Rickettsial Infections

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UNCLASSIFIED

Take Home Points

- Rickettsial infections are:
  - More common than you think
  - Potentially fatal
  - Have non-specific clinical presentations
  - Often require treatment prior to conclusive diagnosis
  - Respond to tetracyclines (Doxycycline)

No one dies of an infectious disease where a Rickettsia may be involved without Doxycycline!

Introduction

- Definitions
  - Rickettsiae: small obligate intracellular bacteria
  - Rickettsioses: diseases caused by rickettsia
- Rickettsia primarily found in arthropods
    - Ticks, mites, lice, fleas, beetles and homopterans
- Only blood-sucking arthropods may transmit disease
- Bacteria invade endothelial cells, cause vasculitis
  - Systemic illness, non-specific presentation
- Rickettsioses increasing in prevalence
  - Increased recognition and diagnostic capacity
  - Changing ecology beneficial to arthropods
  - Increased human/arthropod interface

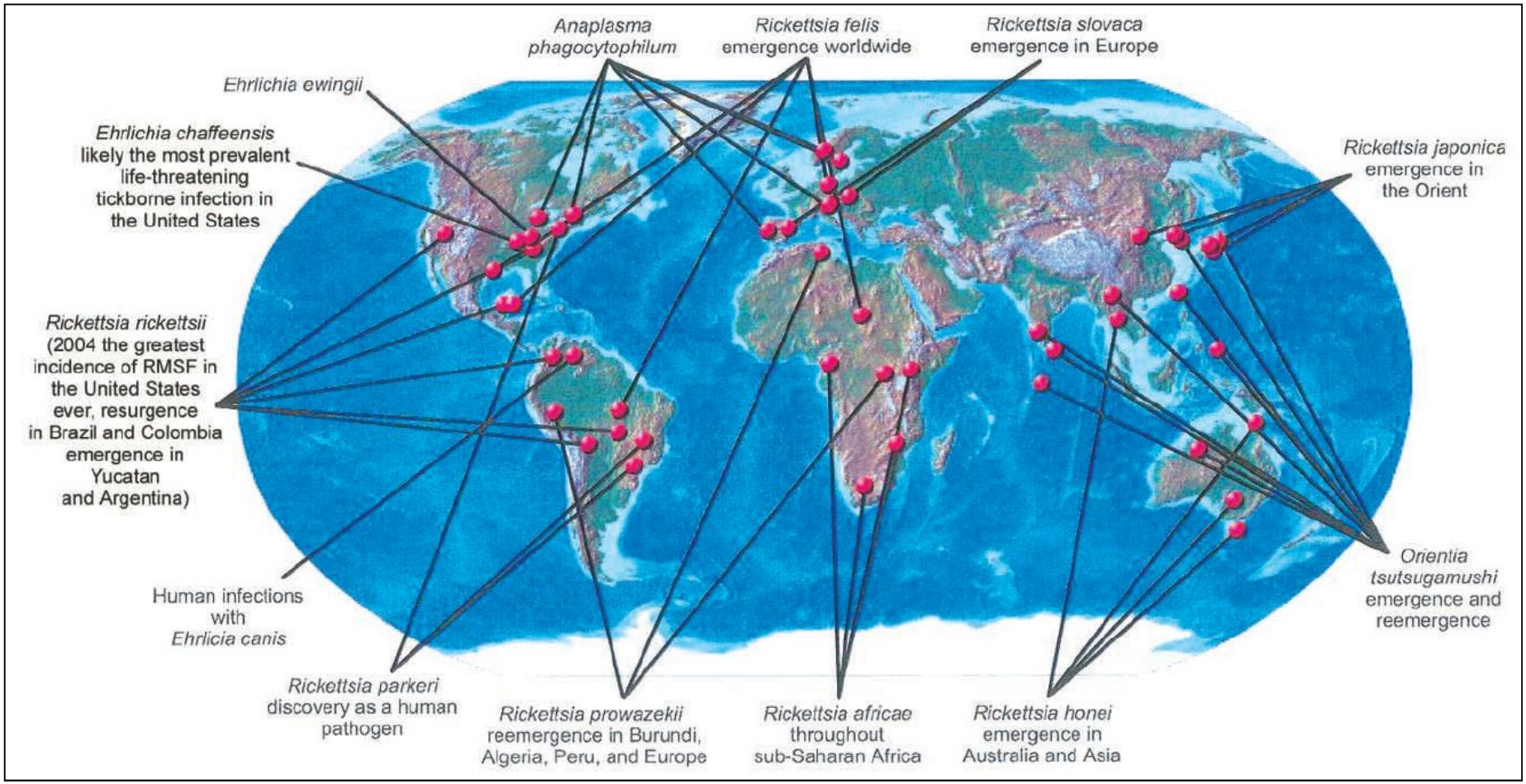
Table 1. Current classification of rickettsioses and their estimated incidence among international travelers.

Classification schemes are constantly evolving.

Biogroup, disease	Species	Principal vectors	Geographic distribution	Incidence among travelers to areas of endemicity
Typhus				
Epidemic typhus	*Rickettsia prowazekii*	Body lice	Central Africa, South America	Very rare
Murine typhus	*Rickettsia typhi*	Rat fleas	Tropical and subtropical areas worldwide	Occasional
Spotted fever				
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Dermacentor* and *Amblyomma* ticks	North and South America	Very rare
Mediterranean spotted fever[a]	*Rickettsia conorii*	*Rhipicephalus* and *Haemaphysalis* ticks	Mediterranean and Caspian littorals, Middle East, Indian subcontinent, Africa	Occasional
Siberian tick typhus	*Rickettsia sibirica*	*Dermacentor* ticks	Northern Asia	Very rare
Unnamed	*Rickettsia sibirica mongolotimonae*	*Hyalomma* ticks	China, France, sub-Saharan Africa	No data
Queensland tick typhus	*Rickettsia australis*	*Ixodes* ticks	Eastern Australia	Very rare
Flinders Island spotted fever	*Rickettsia honei*	Ticks of several genera	Australia, Southeast Asia, northwestern North America	No data
African tick bite fever	*Rickettsia africae*	*Amblyomma* ticks	Sub-Saharan Africa, Caribbean	Common
Japanese spotted fever	*Rickettsia japonica*	Ticks of several genera	Japan	No data
Rickettsialpox	*Rickettsia akari*	Mouse mites	North and South America, Asia	No data
California flea rickettsiosis	*Rickettsia felis*	Cat fleas	Europe, North and South America, Africa, Asia	No data
Unnamed	*Rickettsia heilongjiangensis*	*Dermacentor* ticks	Eastern Asia	No data
Unnamed	*Rickettsia slovaca*	*Dermacentor* ticks	Southern and eastern Europe	No data
Unnamed	*Rickettsia helvetica*	*Ixodes* ticks	Central and northern Europe, Asia	No data
Unnamed	*Rickettsia aeschlimannii*	*Hyalomma* ticks	Mediterranean littoral, Morocco, South Africa	Very rare
Unnamed	*Rickettsia parkeri*	*Amblyomma* ticks	United States	No data
Scrub typhus, scrub typhus	*Orientia tsutsugamushi*	Chigger mites	Southeast Asia, western Oceania	Occasional

[a] Including Astrakhan fever, Israeli tick typhus, and Indian tick typhus.

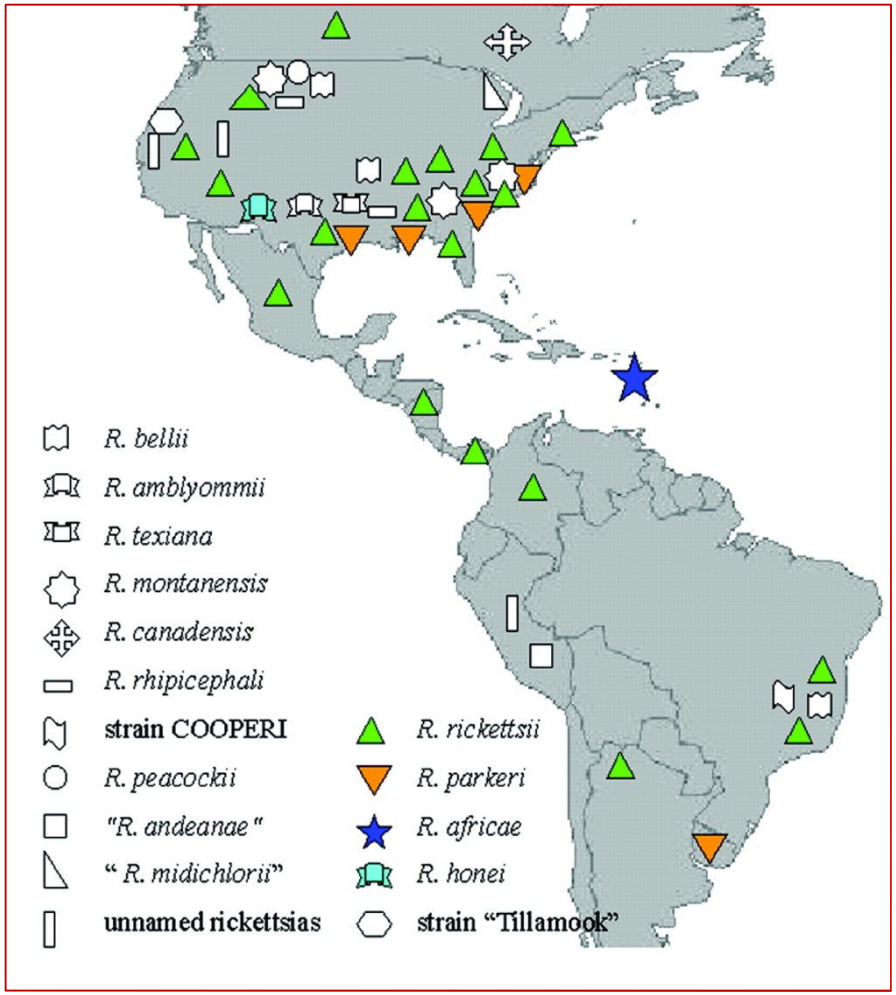
Global Distribution of Rickettsiae, Anaplasma, and Ehrlichia

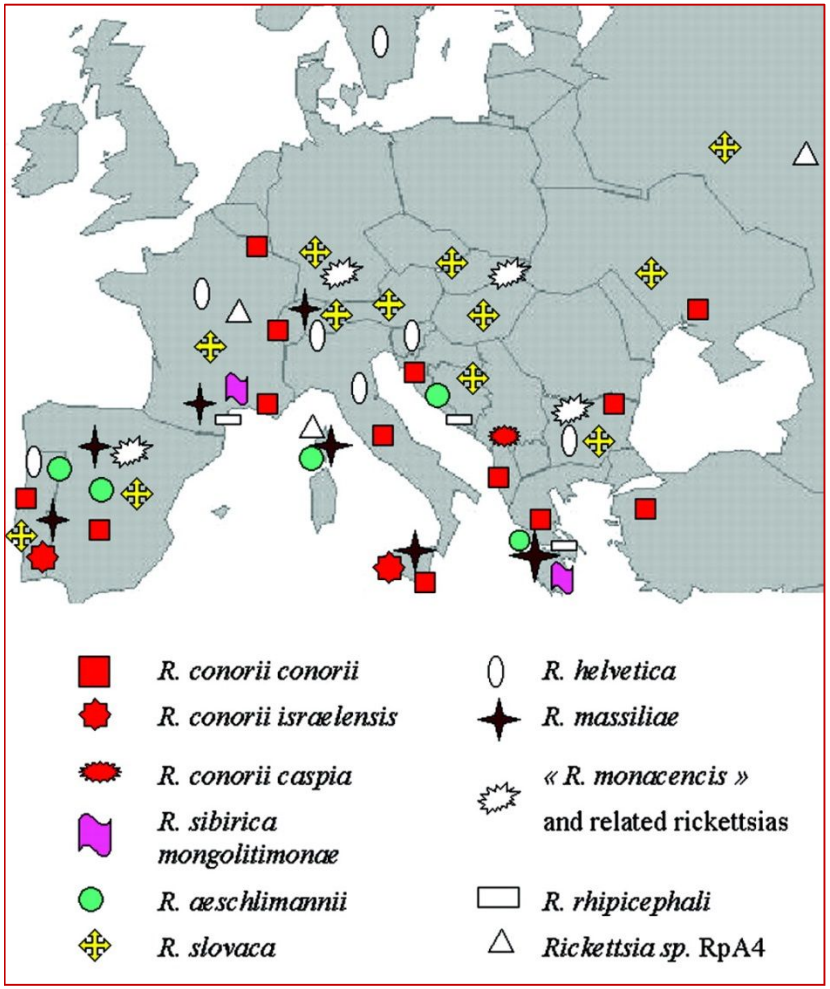


Update on Rickettsial Infections • **CID 2007:45 (Suppl 1)** • S41

Global Distribution of Rickettsiae

(colored shapes = known pathogens)





CLINICAL MICROBIOLOGY REVIEWS, Oct. 2005, p. 719–756
0893-8512/05/$08.00+0 doi:10.1128/CMR.18.4.719–756.2005
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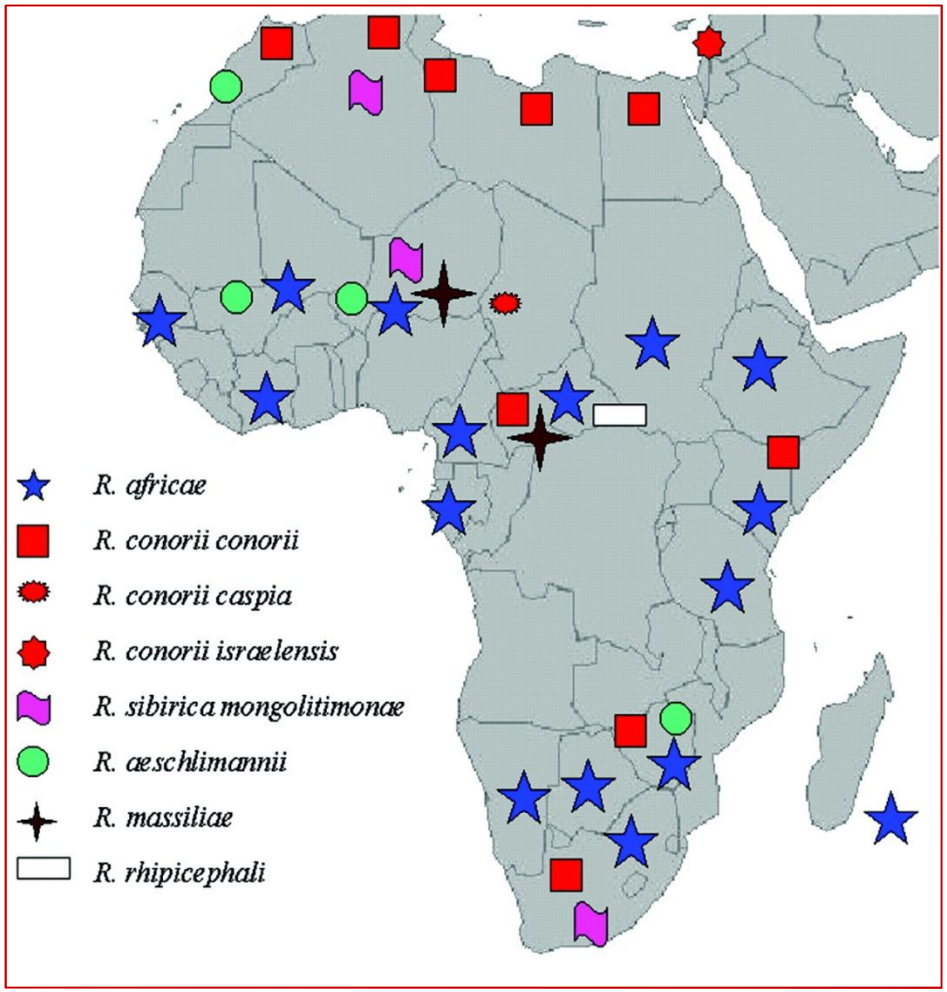
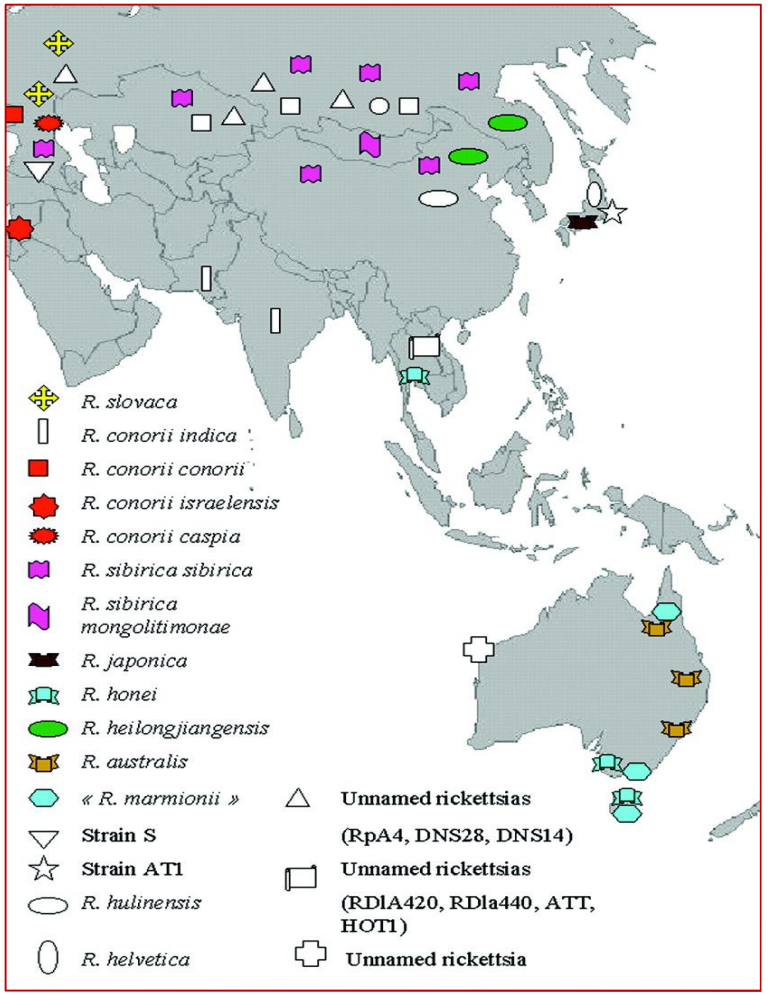
Global Distribution of Rickettsiae

(colored shapes = known pathogens)





CLINICAL MICROBIOLOGY REVIEWS, Oct. 2005, p. 719–756
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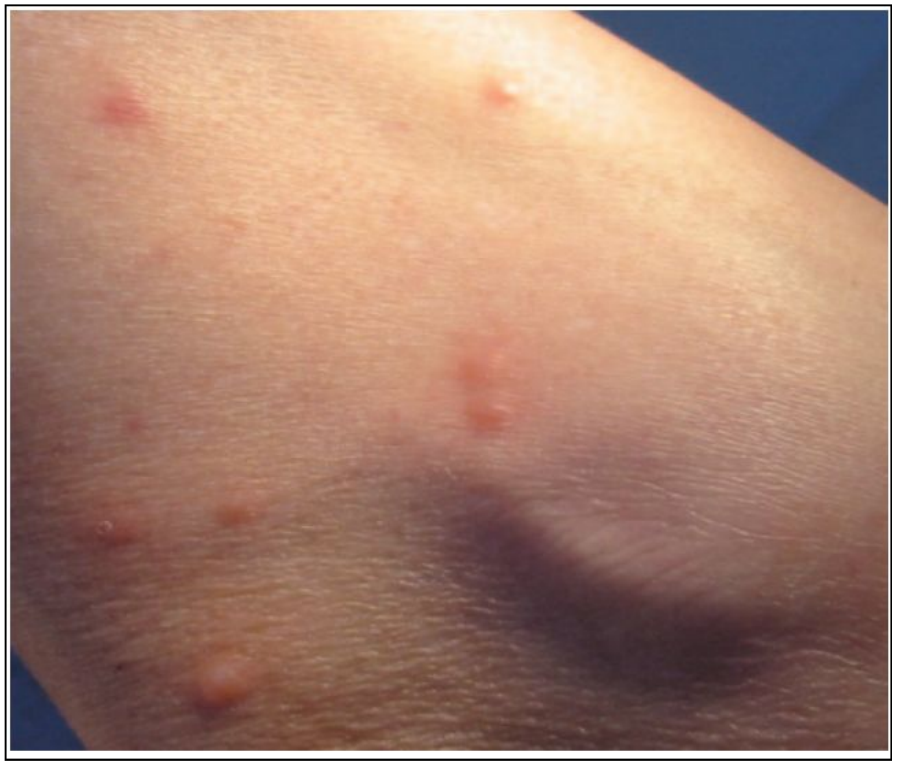
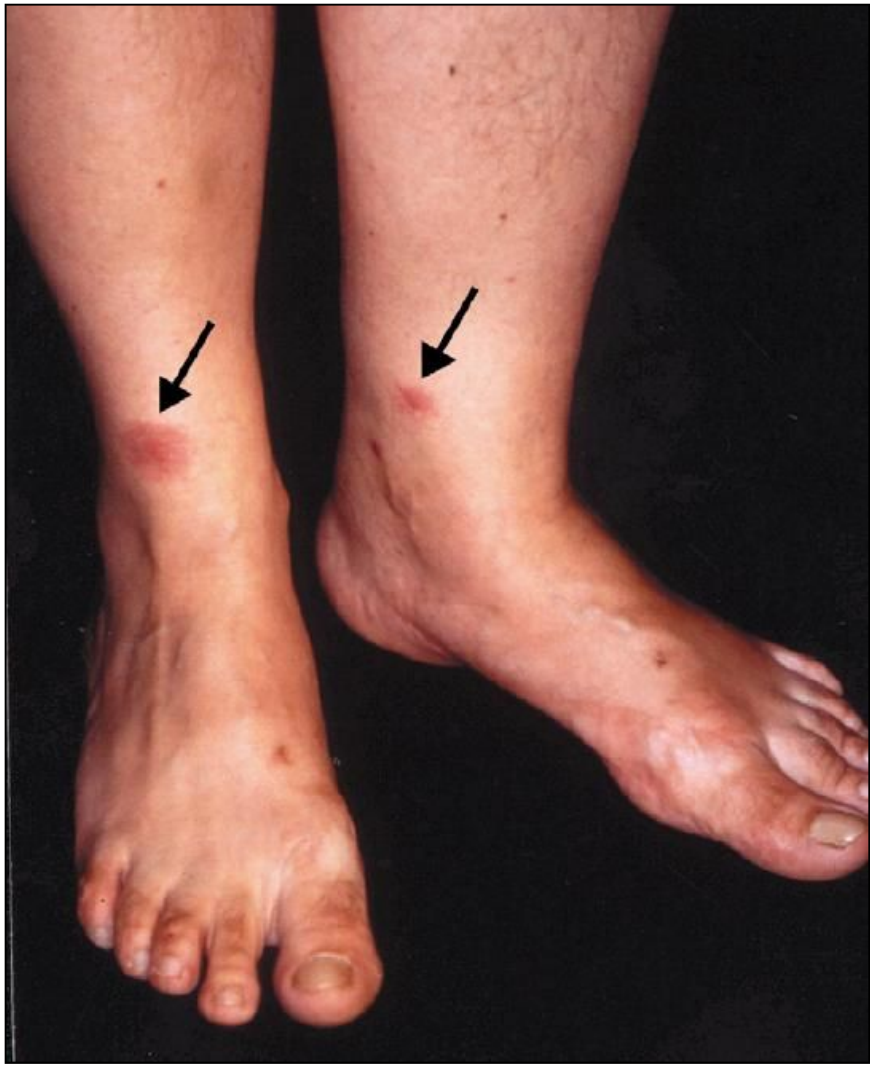
Case #1

- Service Members (SMs) from 2 units are presenting to your clinic with similar illnesses following recent redeployment from Southern Africa (unit #1) and the Caribbean (unit #2).
- Illnesses vary in severity and include symptoms of fever, neck pain, and headache. Exam findings include mouth blisters, vesicular rash, and multiple lesions on the lower extremities (picture). There are enlarged inguinal lymph nodes.
- Some soldiers recall “bug” exposure and many have already recovered from their illness without treatment.

Case #1

Ankle





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Lancet ID 2003;3:557-564

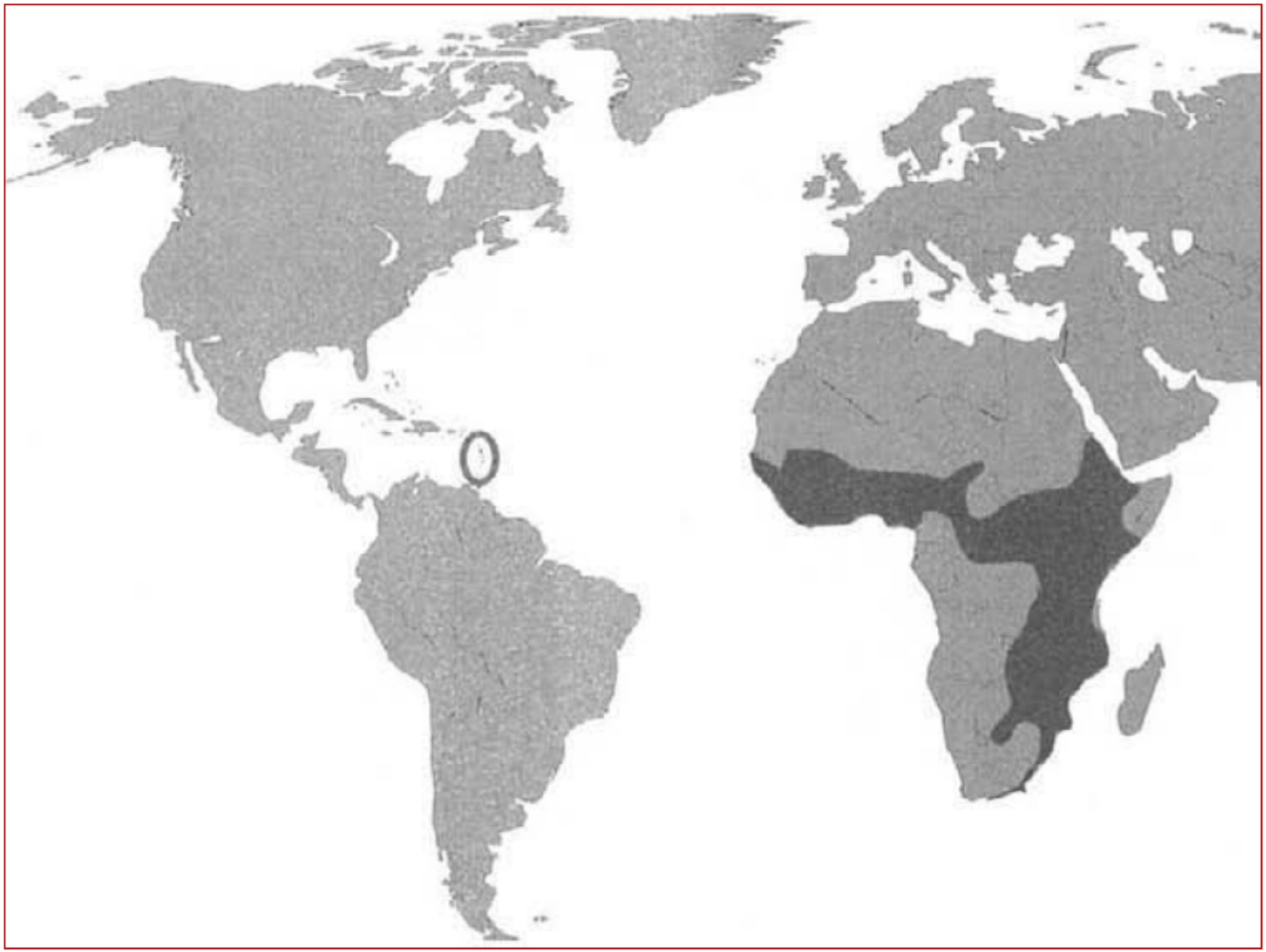
African Tick Bite Fever

- Rickettsia: R. africae
- Ticks
  - Amblyomma hebraeum: Southern Africa
  - A. variegatum: Caribbean
- Epidemiology
  - Men, exposure activities, case clusters
- Illness:
  - Incubation 5-7 days, may be up to 10 days
  - Febrile illness, headache, neck myalgia
  - Rash (50%) (may be vesicular – 50% or rashes)
  - Mouth blisters, regional lymphadenitis
  - ~50% of patients have multiple eschars

Commonalities of Rickettsioses

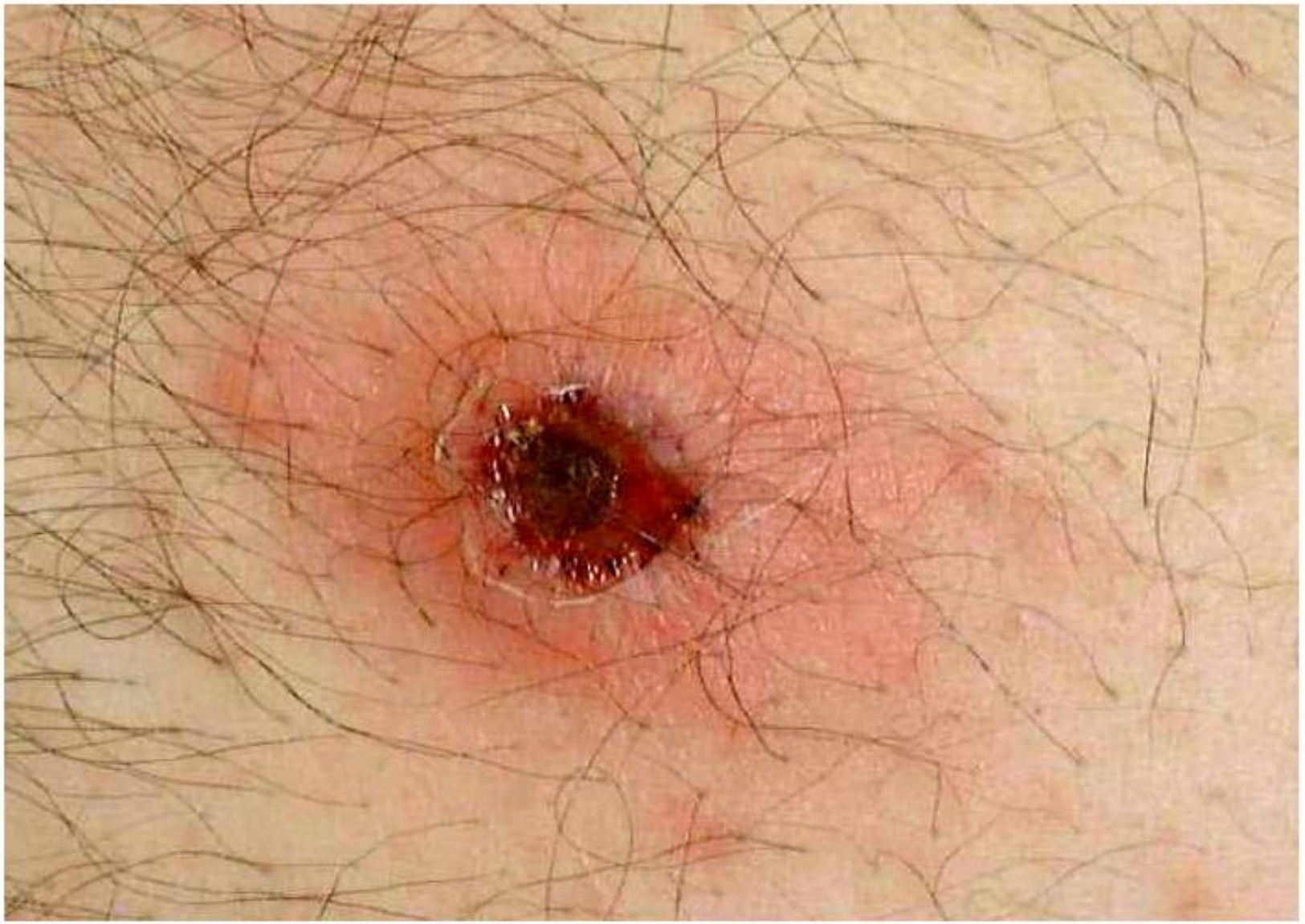
- Fever, headache, +/- rash
- Low WBC, low PLTS, elevated AST/ALT
- Diagnose by serology, immunofluorescence assays, PCR, culture (lab risk)
  - Clinical diagnose is most often required to properly manage the patient. You must make a decision to treat without a definitive diagnosis.
- Tetracyclines are the drugs of first choice for treatment
  - Doxycycline 100 mg po bid x 5 days –or- until 48 hours after defervescence
  - Pregnant women, chloramphenicol, josamycin, or a combination of rifampin and erythromycin

ATBF Distribution



TRAVEL MEDICINE • CID 2004:39 (15 November) • 1495

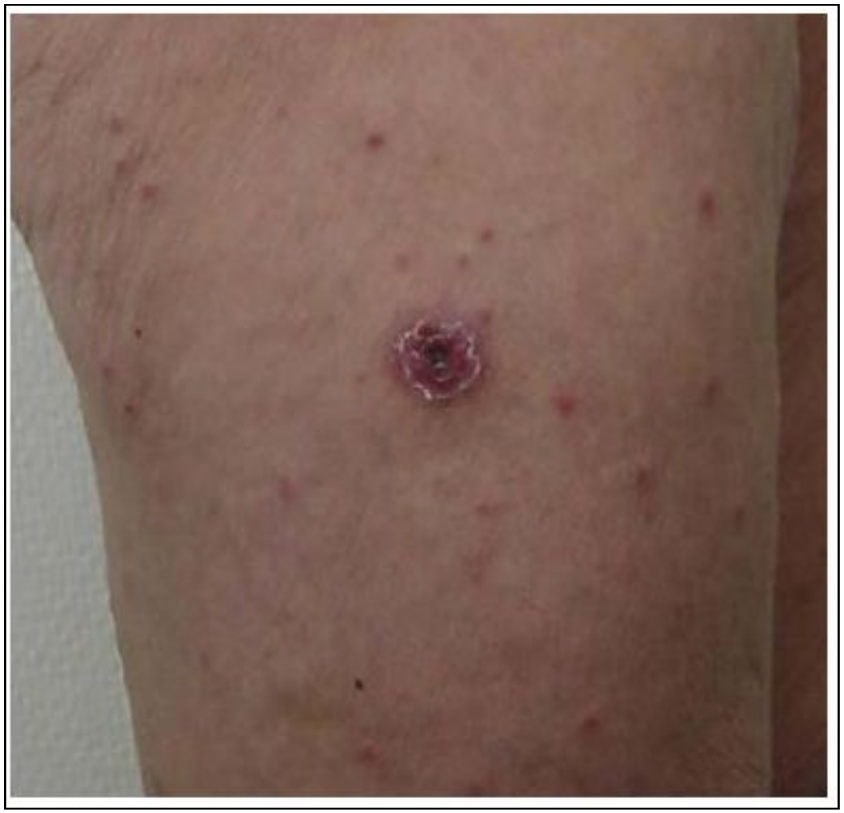
Eschar

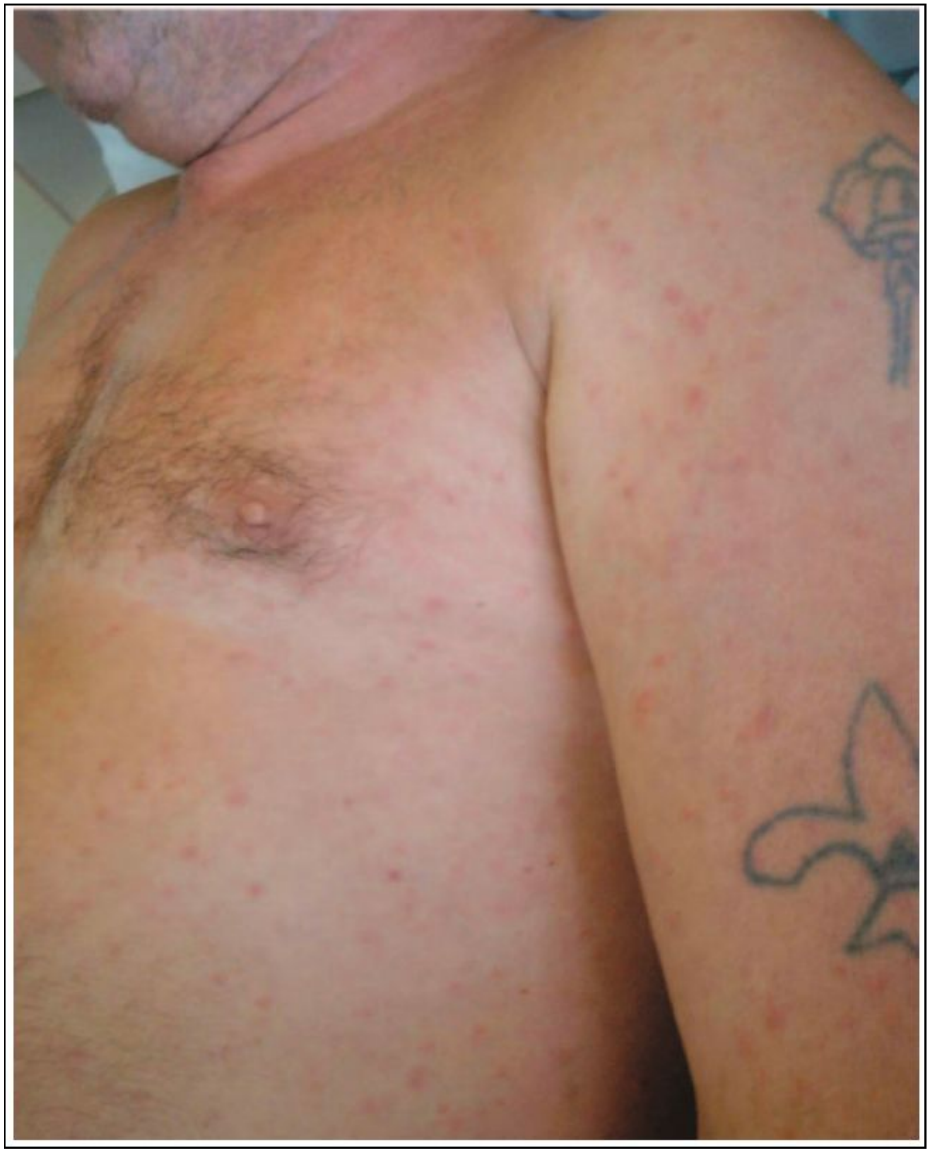


Case #2

- Retired male SM with chronic alcohol dependency presents with high fever, not feeling well, vomiting, a generalized maculopapular rash sparing the face, and an eschar.
- He reports recently returning from a vacation in southern Italy where he stayed at a friend's home and took care of his dogs while the friend was traveling.
- Your examination reveals he is intravascularly deplete and lab values demonstrate multi-organ involvement.

Case #2





Mediterranean Spotted Fever
(Boutonneuse Fever)

- Rickettsia: R. conorii
- Ticks (dog ticks)
  - Rhipicephalus and Haemaphysalis genera
- Epidemiology
  - Mediterranean basin, Middle East, India, expanding
- Illness:
  - Incubation of ~6 days then abrupt onset of symptoms
  - High fever (39°C), flu-like symptoms
  - Single black eschar
  - 1-7 days after fever there is a generalized MP rash
    - Palms and soles but spares the face
  - Recover within 10 days without any sequelae
  - Mortality ~2.5%

Global Distribution of MSF

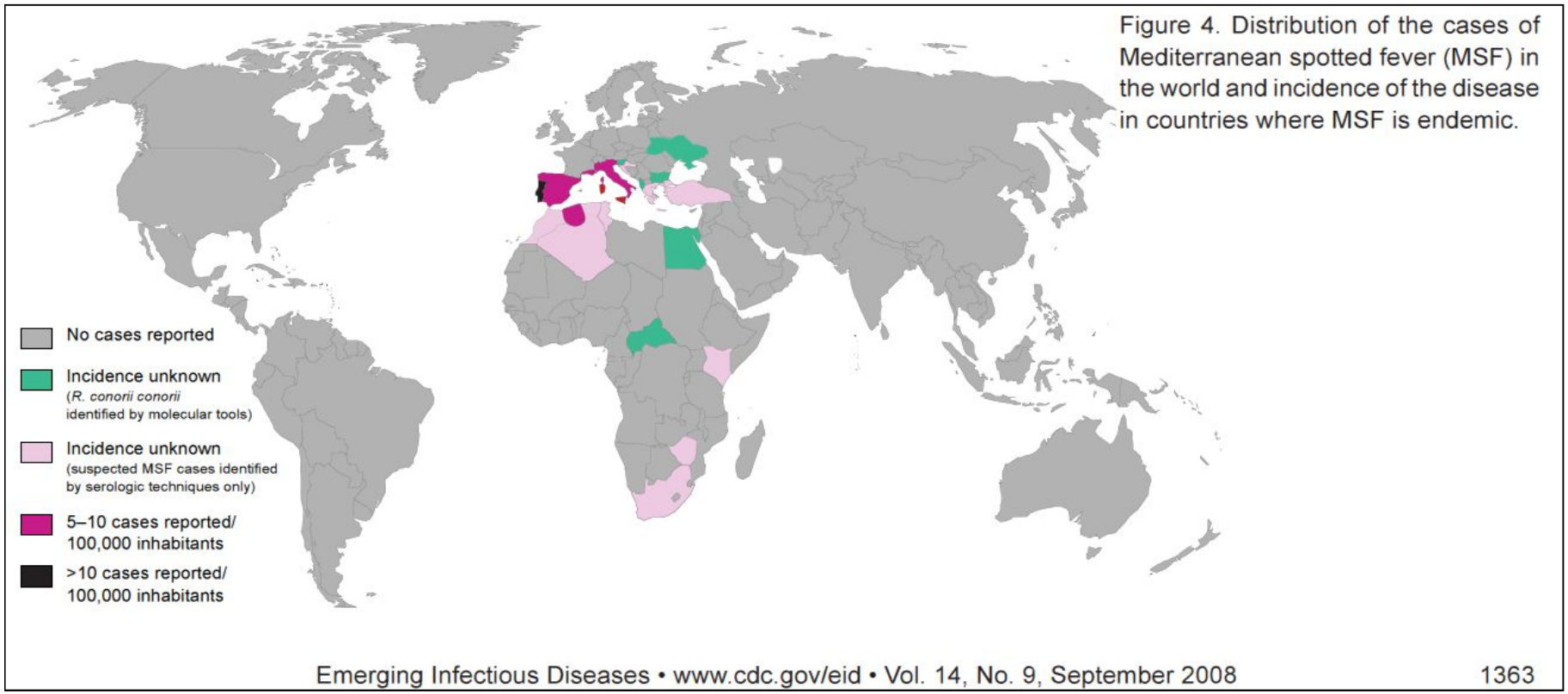


Figure 4. Distribution of the cases of Mediterranean spotted fever (MSF) in the world and incidence of the disease in countries where MSF is endemic.

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R. conorii Complex

Table 2. Distribution, vector, and main clinical features of the different subspecies of *Rickettsia conorii* complex

Rickettsia	Vector tick	Geographic repartition	Human disease name	Symptoms present, % patients			Fatal forms? (% patients)
				Fever	Inoculation eschar	Rash	
R. conorii conorii, isolates Malish, Moroccan Kenyan	*Rhipicephalus* sp., *Haemaphysalis leachii*	Mediterranean area (southern Europe, northern Africa), Croatia, Slovenia, Kenya, Somalia, South Africa, and surrounding the Black Sea (Turkey, Bulgaria, Ukraine, Romania)	Mediterranean spotted fever	91–100	20–87	93–100	Yes (0–18.1)
R. conorii israelensis	*Rh. sanguineus*	Israel, Portugal, Sicily	Israeli spotted fever	100	0–46	98–100	Yes (0–3.5)
R. conorii caspia	*Rh. sanguineus, R. pumilio*	Astrakhan region, Chad, Kosovo	Astrakhan spotted fever	100	23	94	No
R. conorii indica	*Rh. sanguineus, Boophilus microplus, H. leachii*	India, Pakistan	Indian tick typhus	100	Rare	100 (frequently purpuric)	No

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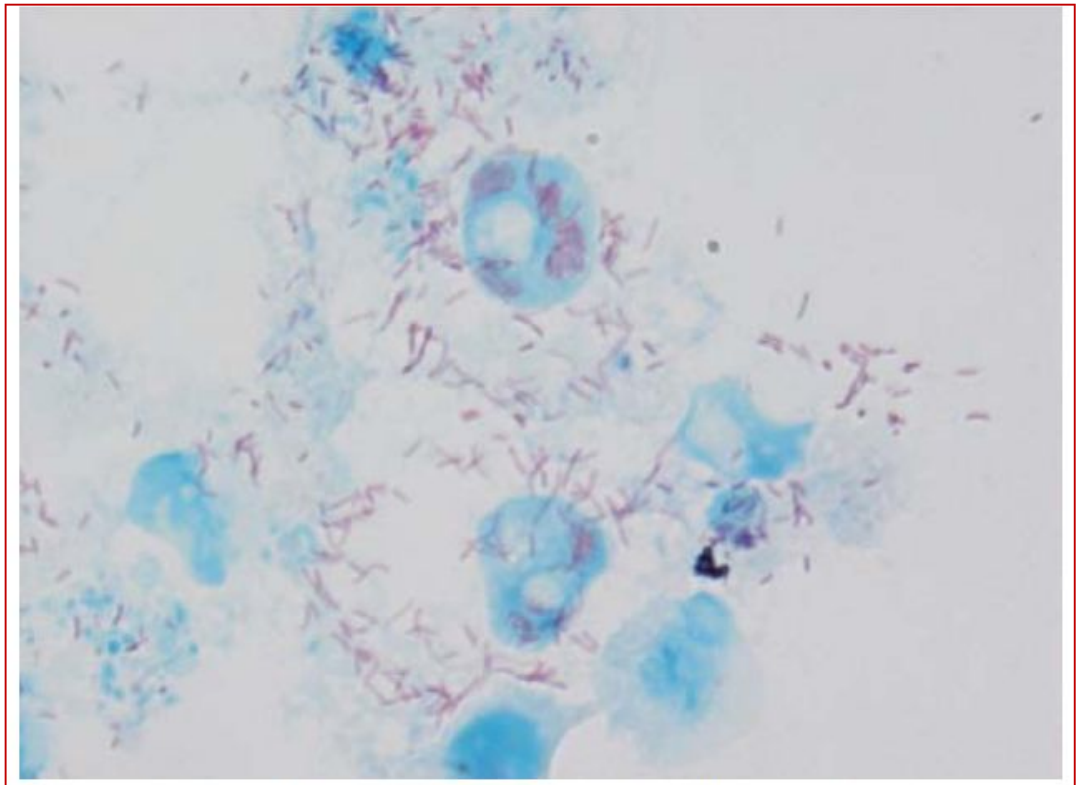


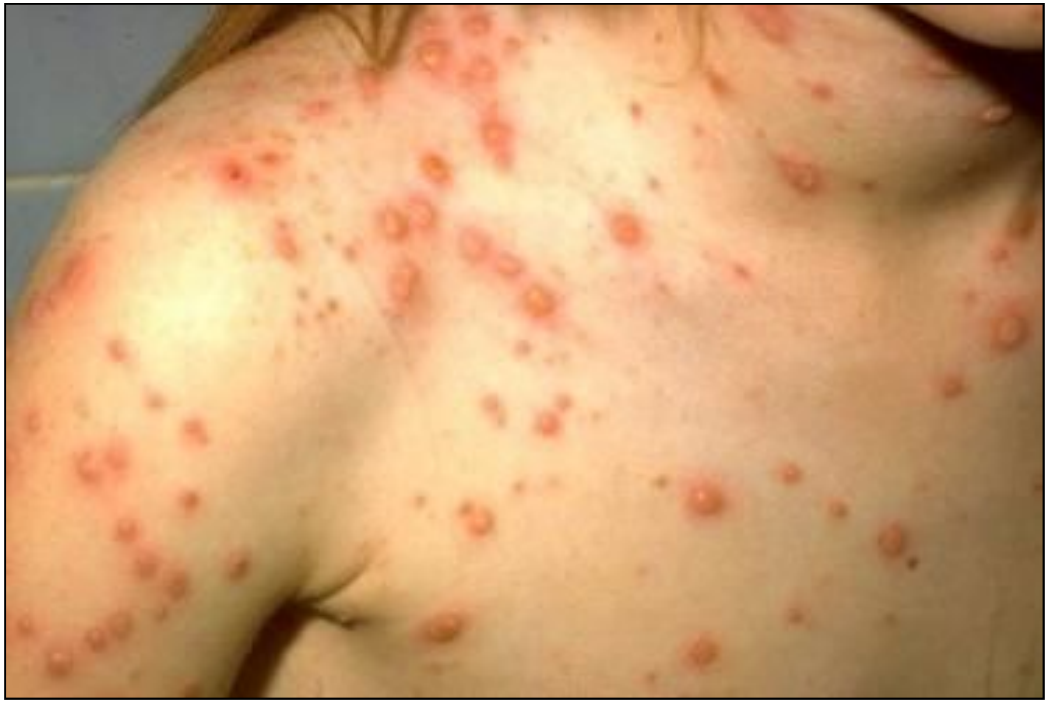
Figure 1. *Rickettsia conorii conorii* in Vero cells (red rods; magnification ×1,000).

Figure 6. *Rhipicephalus sanguineus* adult tick, the suspected vector for *Rickettsia conorii conorii*.

Case #3

- SM develops a fever and rash 3 days into deployment. Additional symptoms include headache, malaise, sweats, and nausea. The rash looks like chicken-pox and there is associated lymph node enlargement.

The SM claims to have had chicken-pox as a child. The SM was on leave in NYC prior to deployment.



Rickettsialpox

- Rickettsia: R. akari
- Mite (mouse)
  - Liponyssoides sanguineus
- Epidemiology
  - NYC, eastern Europe, Korea, and South Africa
- Illness:
  - Incubation 9-14 days
  - Triad of the disease = fever, rash, and eschar
  - Varied constitutional symptoms
  - Papule to vesicle to a brown or dark eschar
  - Rash on day 3 or 4 (papular to vesicular)
  - Self-limited illness (14-21 days)

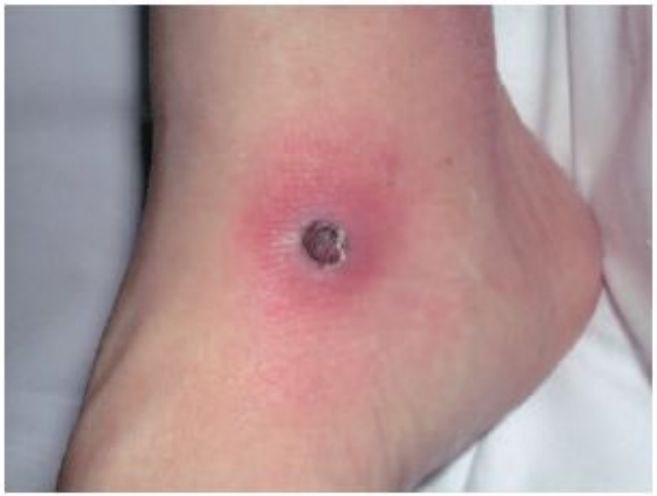


Fig 4. Case 3: Early-stage eschar on right ankle.

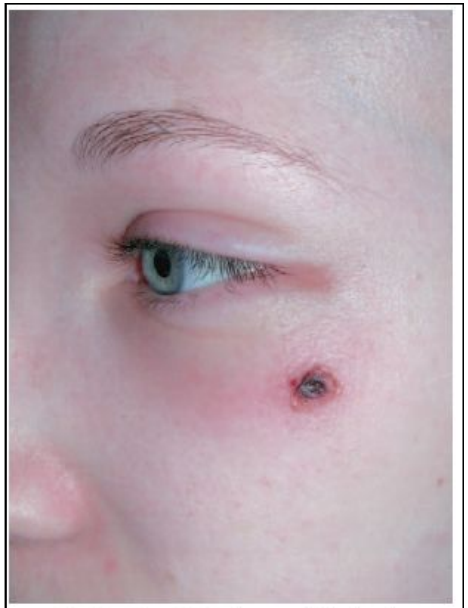


Fig 2. Case 2: Eschar on left cheek.

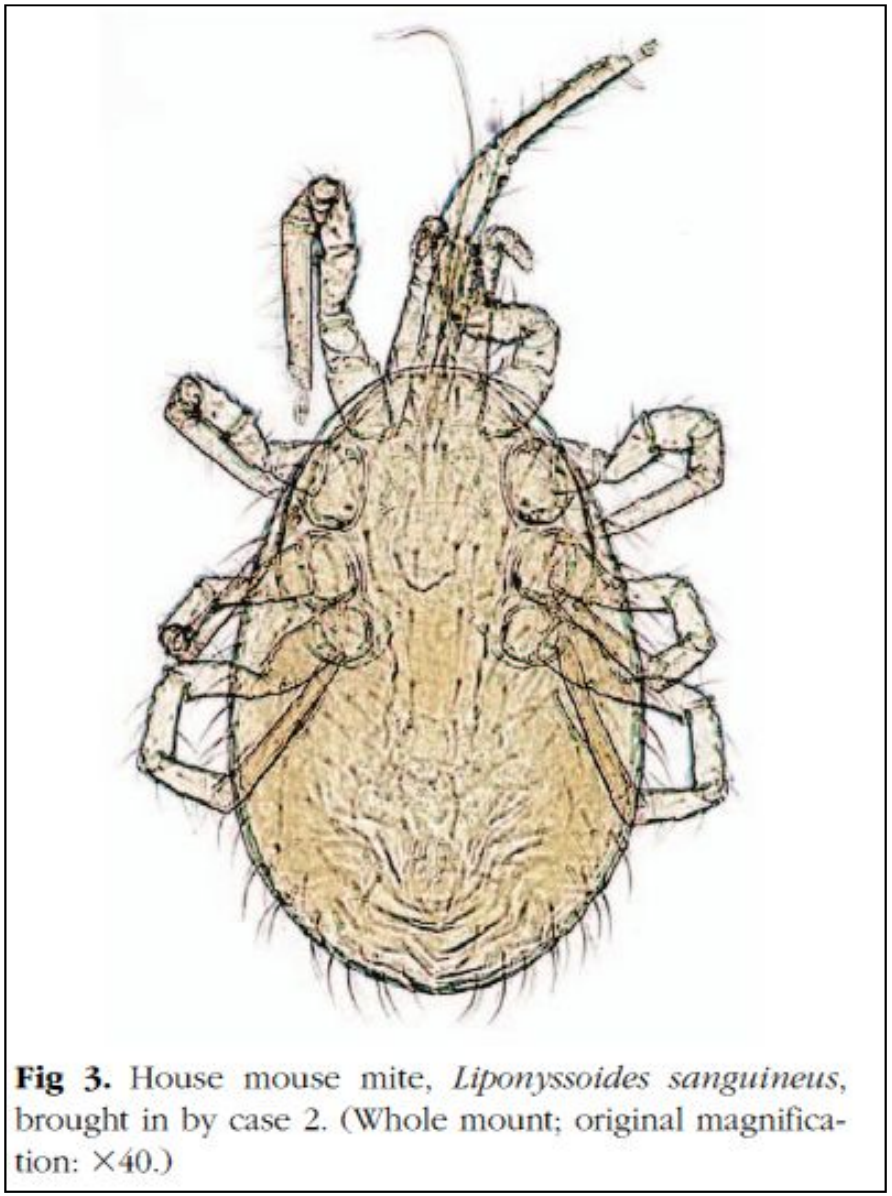


Fig 3. House mouse mite, *Liponyssoides sanguineus*, brought in by case 2. (Whole mount; original magnification: ×40.)

Table III. Distinguishing features of rickettsiaplpox, chickenpox, and smallpox

Feature	Rickettsialpox	Chickenpox[24]	Smallpox (variola major)[25]
Eschar	Yes	No	No
Incubation period	9-14 days	14 days (range 10-23)	12 days (range 10-14)
Prodrome	Usually mild, may be severe. Fever, malaise, and headache.	Absent or mild and brief (less than one day)	Usually severe with high fever, headache, backache. Vomiting and severe abdominal pain may be present. Lasts 2 to 4 days.
Timing and evolution of lesions	Lesion develops at the site of the bite within 24 to 48 hrs and evolves into eschar. Rash begins 2 to 3 days after prodrome. Papules may eventuate in papulovesicles.	Lesions occur in "crops" over 2 to 4 days. Different stages characteristic: macules, papules, vesicles, pustules, crusts	Emerge over 1-2 days and then progress at same rate. The lesions progress over several days from macules (day 1), to papules (day 2), to vesicles (days 3-5), to pustules (days 7-14), to scabs (day 14-20).
Pruritus/ pain	Exanthem usually asymptomatic: occasional pruritus.	Commonly pruritic	Pruritic during healing, otherwise may be painful.
Distribution	Anywhere. Palms, soles not usually involved.	Starts on trunk and face and spreads centrifugally. Palms, soles may be involved	Begins on the oral mucosa, face, and extremities and spreads centripetally. Palms, soles commonly involved.
Enanthem	Minority of cases.	Common, especially palate.	Starts in mouth
Scarring	Eschar leaves depressed scar, papulovesicles do not.	If bacterial superinfection occurs	Yes

Case #4

- SM serving in Central America on a humanitarian mission presents after 3 days of an evolving illness to include fever, headache, fatigue, and abdominal discomfort.
- He has no medical or surgical history. He smokes and uses alcohol infrequently. He lives in a private room and has no sick contacts. All water, to include ice and brushing teeth, is from bottles. He occasionally eats on the economy but has not done so for 3 weeks. During the past 4 weeks he has been conducting missions in rural villages. He recalls no insect exposure. He declines to provide a sexual activity history.
- On exam he is febrile (38C) and appears ill. You notice a few macules on his palms.

Rocky Mountain Spotted Fever

- Rickettsia: R. rickettsii
- Tick (dog)
  - Dermatocenter, Rhipicephalus
- Epidemiology
  - US, Southern Canada, Mexico, C. and S. America
- Illness:
  - Does not generally elicit an eschar
  - High fever, headache, malaise, myalgias, nausea, vomiting, anorexia, abdominal pain, and diarrhea
  - RMSF rash is usually not apparent until the third day
    - Small, irregular, pink macules, peripheral → central
    - Classic spotted rash (50%) not until day 5 = severe
  - MOST SEVERE Rickettsioses (fatal in 5% or greater)

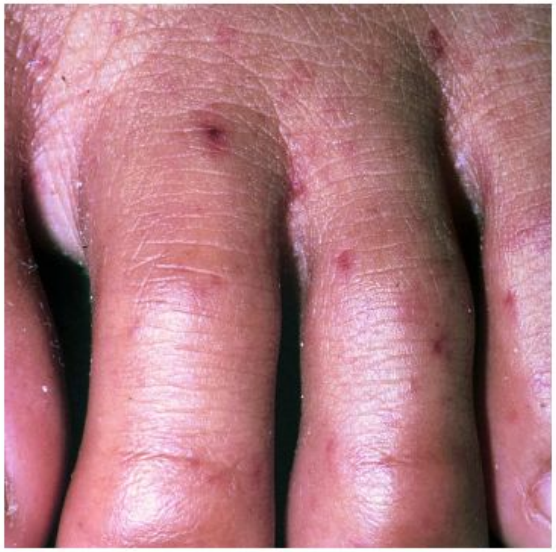
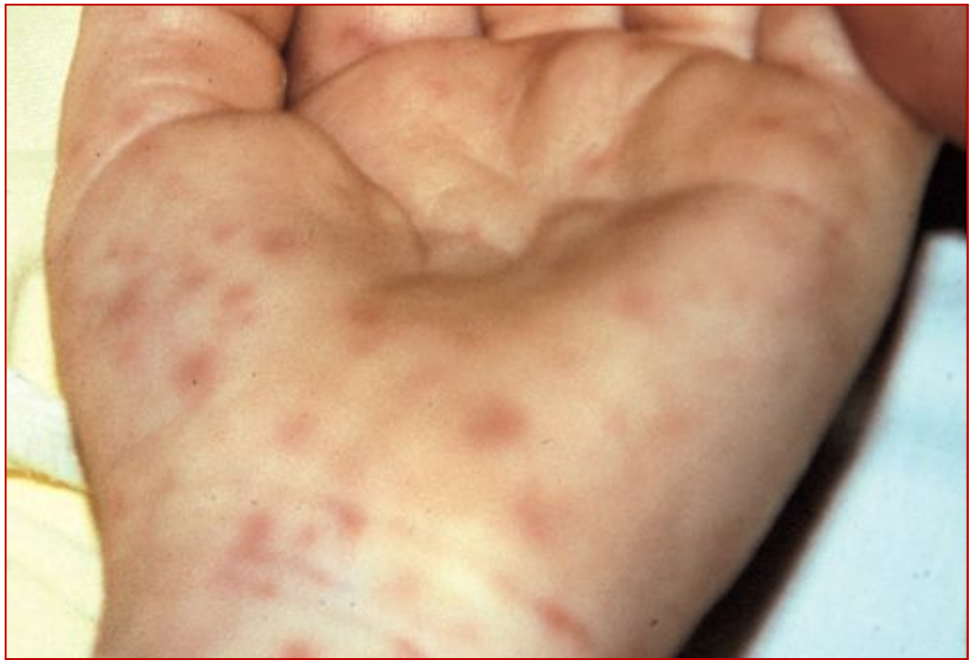
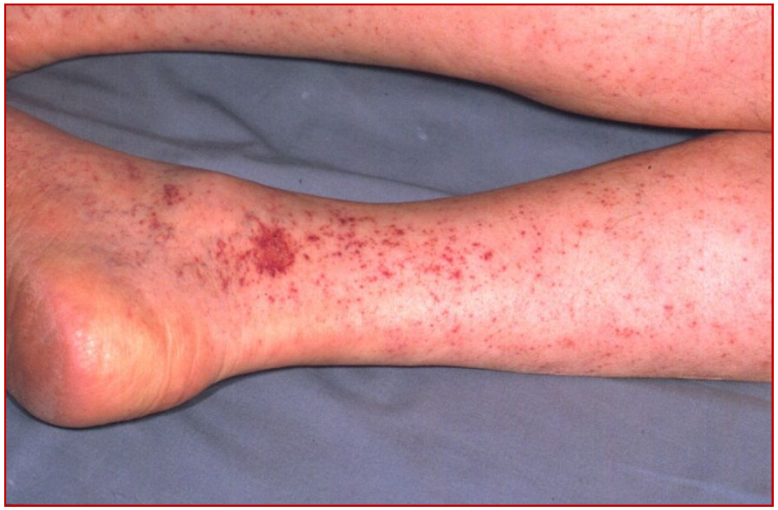


Fig. 2 Acral petechial rash of Rocky Mountain spotted fever (reprinted with permission from Brooke Army Medical Center Teaching File).





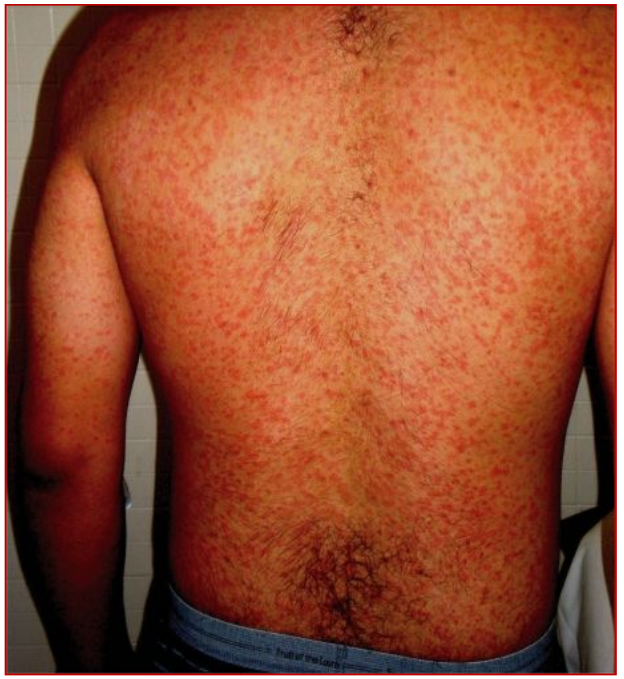
Rock Mountain Spotted Fever

Case #5

- SM presents with headache and fever following leave in Mexico. Review of systems indicates associated nausea, vomiting, and new onset cough. You appreciate hepatomegaly and confusion on examination.
- A travel history indicates he was in Mexico for 1 week with a group of friends. He stayed at economy hotels and hostels. He stated the rooms were clean but the neighborhoods were in some disrepair with garbage on the street; he noticed numerous rodents. There were no sexual exposures and no use of drugs. He had no animal exposures. Food and water were on the economy.

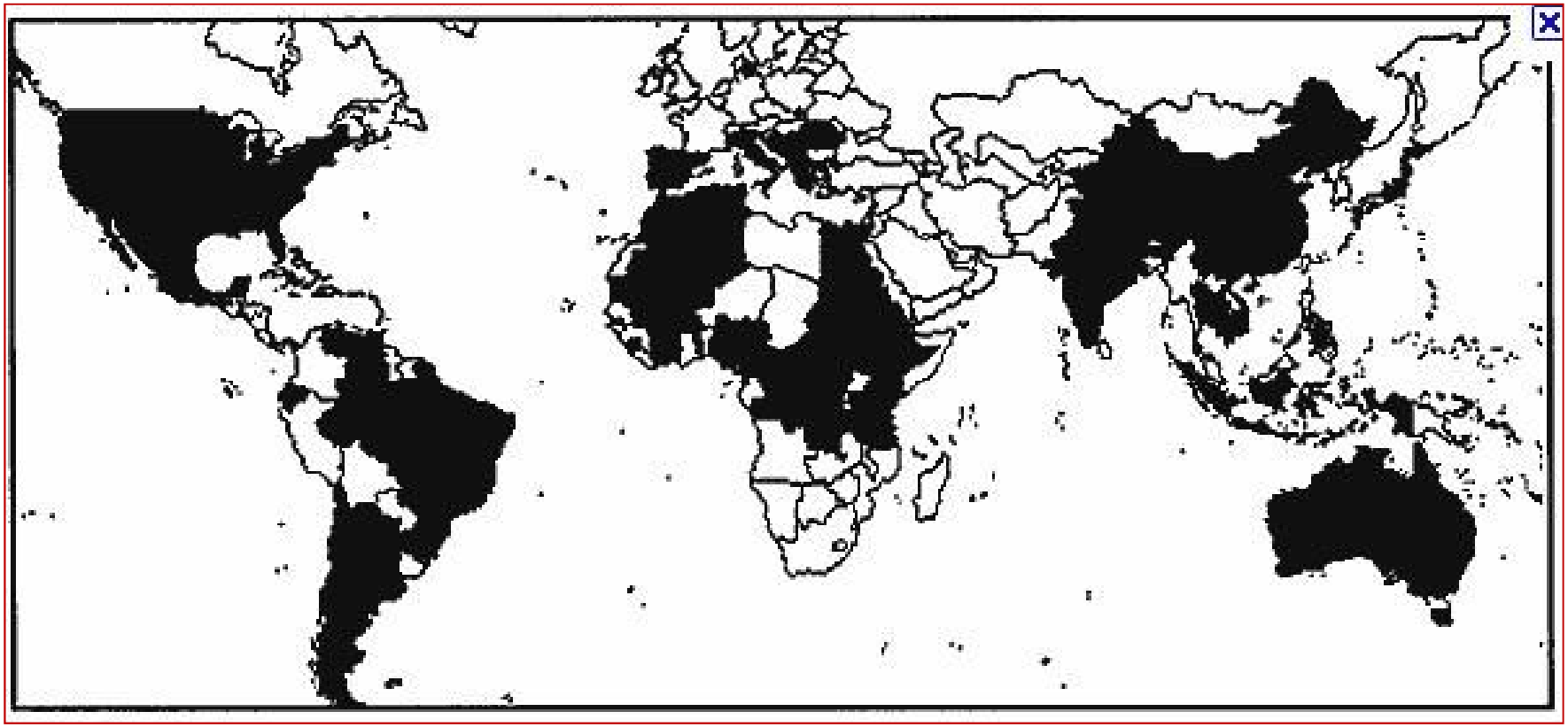

TAVERNA

Murine Typhus (endemic)



- Rickettsia: R. typhi
- Flea (rat)
  - Xenopspylla cheopis
- Epidemiology
  - United States, Mexico, Europe
- Illness:
  - 6-14 day incubation period
  - Fever and headache, rash less often
  - Nausea, vomiting, abdominal pain, diarrhea, jaundice, cough, confusion, and seizures have been reported
  - Typically a self-limited illness

R. typhi Global Distribution



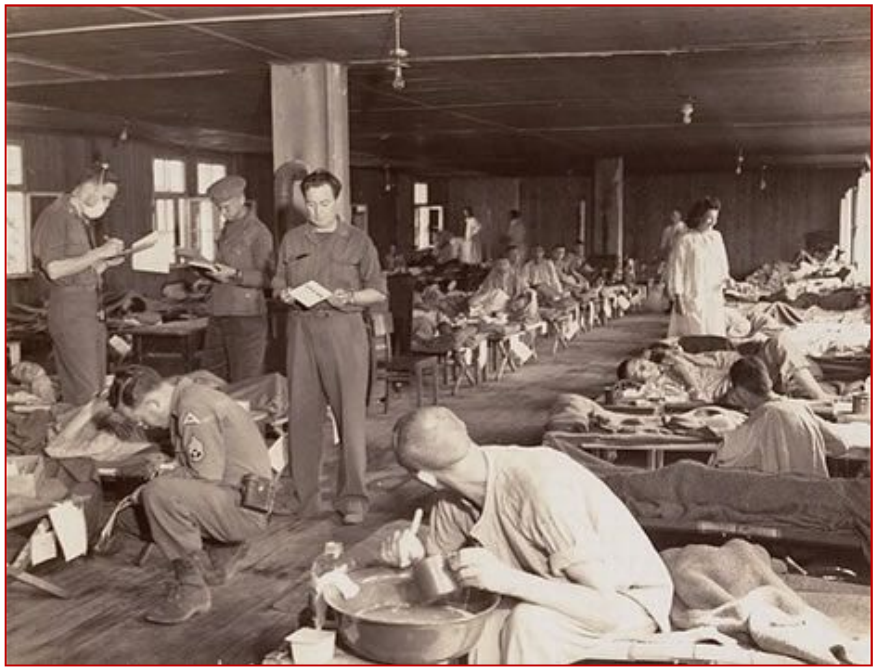
Case #6

- SM on mission in Africa (Burundi) presents with fever, headache, and confusion. His duties while on mission included working at a refugee camp for displaced persons. The SM had very close contact with refugees in his day to day duties of supporting sustainment operations. He states other people were also sick and some had died before they could access care.

Epidemic Typhus

- Rickettsia: R prowazekii
- Flea (body lice): Pediculus humanus humanus
- Epidemiology
  - Africa (Ethiopia, Nigeria, Burundi), Mexico, Central America, South America, Eastern
  - War, refugees, prison, close quarters, bad hygiene
- Illness:
  - Incubation 10-14 days
  - Malaise, F, headache, myalgia, N, V, coughing, rash
  - Confusion, stupor, coma, diarrhea, pulmonary involvement, myocarditis, splenomegaly
  - Case fatality rate: 4%
- Brill-Zinsser disease: Recrudescence months to years

Epidemic Typhus



Epidemic Typhus

- Only typhus group with humans as usual host
- Crowded, war/disasters, lacking water; body lice

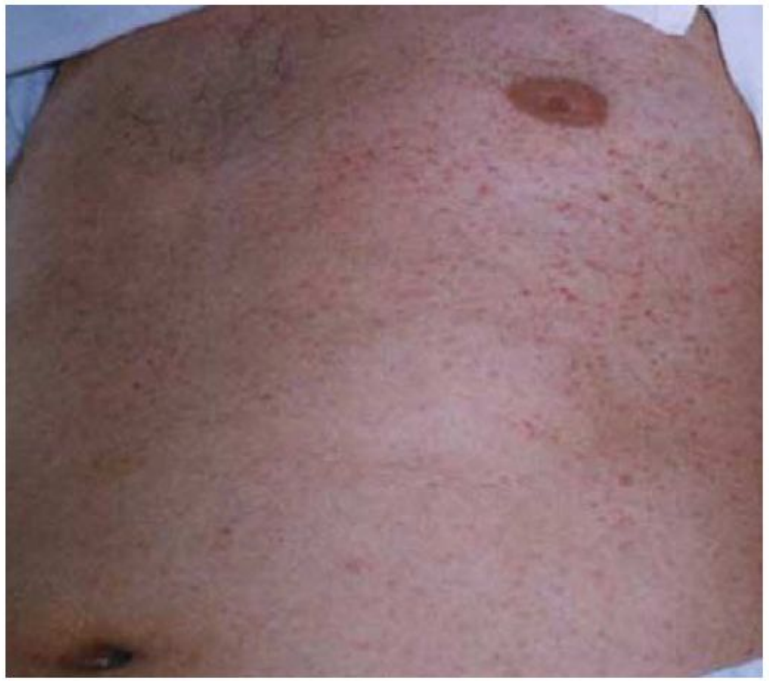


Fig. 4 Eruption in a patient with epidemic typhus imported from Algeria to France (from Ref. [39]).

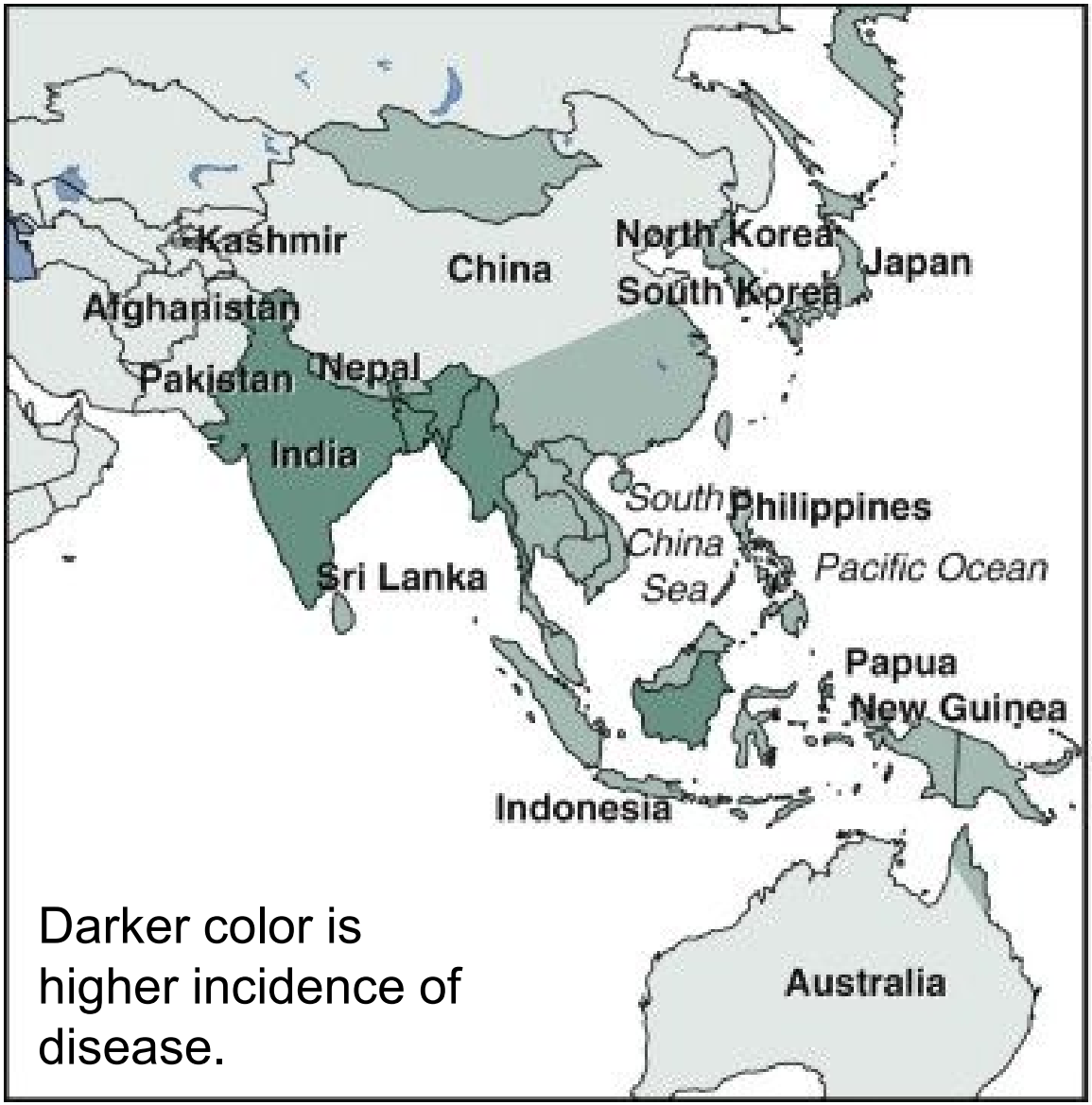
Case #7

- Young female presented with fever, lymphadenopathy and a faint rash after a 2 week trek in the Northern territory of Thailand. She was treated with Doxycycline for 5 days, 200mg po qd. Her symptoms continued and worsened, she now has N, V, abdominal pain and a new cough.

Scrub typhus

- Rickettsia: Orientia tsutsugamushi
- Larval trombiculid mites: chiggers
- Epidemiology
  - Asia-Pacific, Korea to Papua New Guinea, Australia and from Japan to India and Afghanistan
  - Rural exposures, agriculture
- Illness:
  - Incubation 7 - 10 days
  - Papule at the bite site, ulcerates, forms eschar
  - Fever, lymphadenopathy, M or MP rash, headache, myalgia. GI and respiratory symptoms are frequent.
  - Asymptomatic infection to fatal (30%) (strain)
  - DOXY MAY BE RESISTANT IN THAILAND
    - Azithromycin or rifampin

Scrub typhus Distribution



Darker color is higher incidence of disease.

Figure 4. Typical area of scrub typhus endemicity in Thailand

Prevalence of Signs and Symptoms

	Phongmany[5a]	Tattersall[4]
Year	2006	1945
Number of cases	31	500
Location	Laos	India, Burma
Population	Local residents	Soldiers and local residents
Signs and Symptoms		
Fever	100%	
Mental changes		100%
Headache	95%	100%
Cough	38%	68%
Myalgia	95%	
Nausea	62%	
Adenopathy	59%	92%
Eschar	52%	11%
Splenomegaly	59%	47%
Rash	27%	64%
Case-fatality rate	1.5%	6%

Scrub typhus

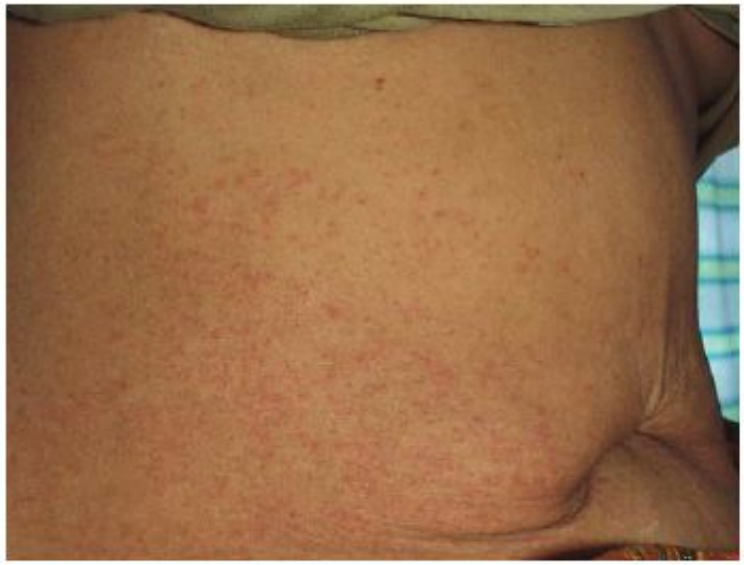
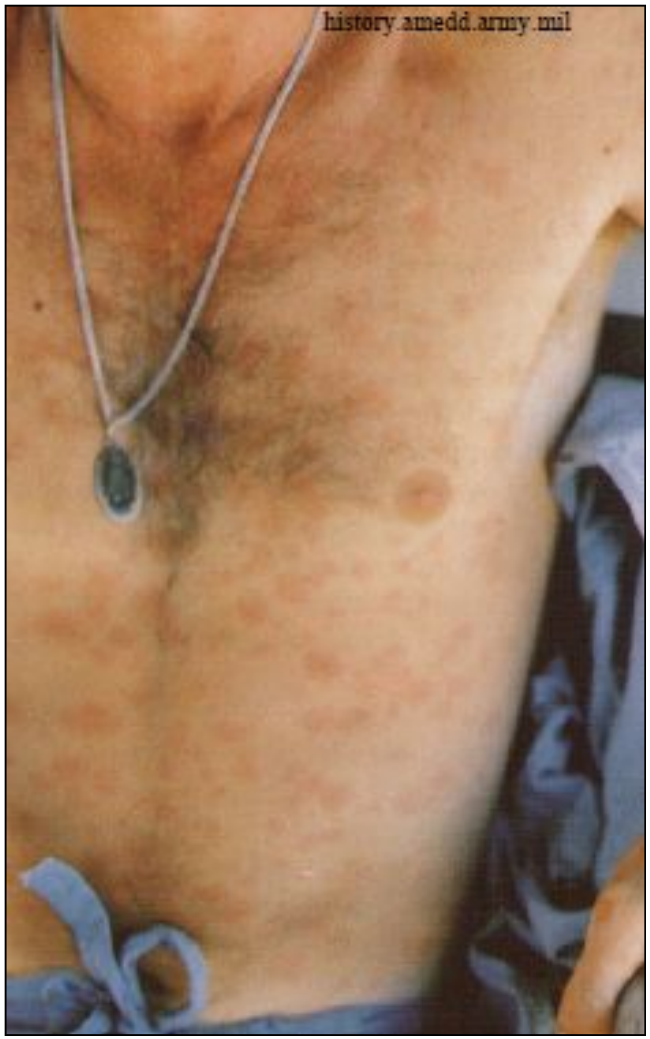


Fig. 6 Macular eruption in a patient with scrub typhus (from Ref. [44]).

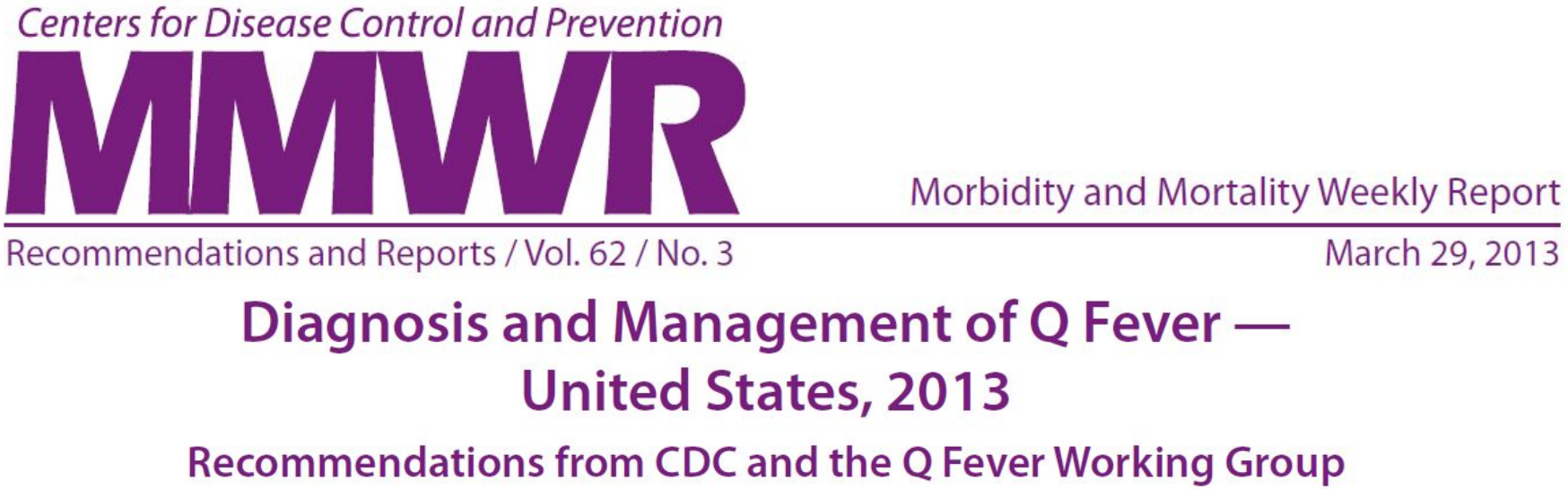


Non-rickettsial illnesses
Similar presentations and treatment

(urban) Trench Fever

- *Bartonella quintana*
  - originally *Rickettsia quintana*
- Napoleon's Grand Army, WWI, WWII
- Human body louse - *Pediculus humanus*
  - Infected feces or crushed louse into broken skin
  - Aerosol to mucous membranes
- Densely populated, poverty-stricken areas of Africa, Latin America, Eastern Europe
- Bacteremia, bacillary angiomatosis, parenchymal peliosis
  - More severe in immunocompromised

Q fever (*Coxiella burnetii*)



- Q = Query
- Worldwide distribution (↓ USA, ↓↓ New Zealand)
- Infectious particles inhaled or ingested
- 1 organism can cause clinical infection
- Incubation 2-3 weeks

Q Fever Risk Factors

- Increased contact with animals or animal products (particularly livestock), including veterinarians, butchers, slaughterhouse workers, farmers, and laboratory workers
- Living in a rural area or living on or within 10 miles of a farm
- Travel to areas of higher risk for Q fever, recent outbreaks
- Sexual contact with a person who has recently had Q fever
- Contact with contaminated clothing and linens
- Q fever symptoms in a person who has a partner or family member who has received a diagnosis of Q fever
- Chronic Q fever symptoms in anyone with a history of acute Q fever infection, particularly persons with valvular heart disease or a vascular graft or arterial aneurysm, immunosuppressed persons, and women who are pregnant

TABLE 3. CDC surveillance case definition and case classification for acute and chronic Q fever

	Acute Q fever	Chronic Q fever
Clinical evidence of infection	Fever and one or more of the following: rigors, severe retrobulbar headache, acute hepatitis, pneumonia, or elevated liver enzymes	Newly recognized culture-negative endocarditis (particularly in a patient with previous valvulopathy or compromised immune system), suspected infection of a vascular aneurysm or vascular prosthesis, or chronic hepatitis, osteomyelitis, osteoarthritis, or pneumonitis in the absence of other known etiology
Laboratory criteria*,†	**Laboratory confirmed (one or more of the following):** • Fourfold change in IgG antibody titer to *Coxiella burnetii* phase II antigen by IFA between paired sera • Detection of *C. burnetii* DNA in a clinical specimen by PCR • Demonstration of *C. burnetii* in a clinical specimen by IHC • Isolation of *C. burnetii* from a clinical specimen by culture	**Laboratory confirmed (one or more of the following):** • IgG titer ≥1:800§ to *C. burnetii* phase I antigen by IFA • Detection of *C. burnetii* DNA in a clinical specimen by PCR • Demonstration of *C. burnetii* in a clinical specimen by IHC • Isolation of *C. burnetii* from a clinical specimen by culture
	Laboratory supportive (one or more of the following): • Single IgG titer ≥1:128 to *C. burnetii* phase II antigen by IFA (phase I titers may be elevated as well) or • Elevated phase II IgG or IgM antibody reactive with *C. burnetii* antigen by ELISA, dot-ELISA, or latex agglutination	**Laboratory supportive:** • IFA IgG titer ≥1:128 and <1:800§ to *C. burnetii* phase I antigen
Case classification	**Confirmed acute Q fever:** Laboratory-confirmation with clinical evidence of infection or an epidemiological link to a laboratory-confirmed case **Probable acute Q fever:** Clinical evidence of infection with laboratory-supportive results	**Confirmed chronic Q fever:** Clinical evidence of infection with laboratory confirmation **Probable chronic Q fever:** Clinical evidence of infection with laboratory-supportive results

Abbreviations: ELISA = enzyme-linked immunosorbent assay; IFA = indirect immunofluorescence antibody assay; IgG = immunoglobulin G; IgM = immunoglobulin M; IHC = immunohistochemistry; PCR = polymerase chain reaction.

* CDC prefers simultaneous testing of paired samples. IgM tests are not strongly supportive of serodiagnosis because the response might be persistent (making it unreliable as an indicator of recent infection) or nonspecific (resulting in false positives). ELISA tests are not quantitative and cannot be used to measure changes in antibody titer; thus, they can only be used for classification of probable cases. Performing laboratories determine the appropriate cutoff titers for ELISA. Serologic test results should be interpreted with caution because baseline antibodies acquired as a result of previous exposure to Q fever might exist, especially in patients with rural or farming backgrounds.

† Patients with suspected chronic Q fever should be evaluated for titers both to phase I and phase II antigens. Serologic test results should be interpreted with caution because baseline antibodies acquired as a result of previous exposure to Q fever might exist, especially in patients with rural or farming backgrounds.

§ U.S. laboratories use a twofold dilution scheme that does not result in a titer equaling 800; in this document, a titer of 1024 is used as the replacement.

TABLE 1. Percentage of acute Q fever patients with selected clinical and laboratory findings

Clinical or laboratory finding	% of patients
Clinical	
Fever	88–100
Fatigue	97–100
Chills	68–88
Headache	68–98
Myalgia	47–69
Sweats	31–98
Cough	24–90
Nausea	22–49
Vomiting	13–42
Chest pain	10–45
Diarrhea	5–22
Skin rash	5–21
Myocarditis	0.5–1
Pericarditis	1
Meningoencephalitis	1
Death	1–2

Clinical or laboratory finding	% of patients
Laboratory	
Normal leukocyte count	90
Thrombocytopenia	25
Increased transaminase levels*	45–85
Increased bilirubin levels	9–14.3
Increased alkaline phosphatase levels	27.7–57
Increased γ-glutamyl transferase levels	25–75
Increased creatine phosphokinase levels	29
Increased lactate-dehydrogenase levels	33.3–40
Increased creatinine levels	29–40
Elevated erythrocyte sedimentation rate	43–87.5
Smooth muscle antibodies	65
Antiphospholipase antibodies	50

Source: Modified from Maurin M, Raoult D. Q fever. Clin Microbiol Rev 1999;12:518.

* Alanine transaminase and aspartate transaminase.

Summary of Acute Q Fever

- Prolonged fever (>10 days) with a normal leukocyte count, thrombocytopenia, and increased liver enzymes is suggestive of acute Q fever infection.
- Children with Q fever generally have a milder acute illness than adults.
- Children are more likely to have a rash than adults. Rash has been reported in up to 50% of children with acute Q fever.
- Women infected with Q fever during pregnancy are at increased risk for miscarriage and preterm delivery.
- Women of child-bearing age who receive a diagnosis of Q fever can benefit from pregnancy screening and counseling to guide health-care management decisions

Summary of Chronic Q Fever

- Persons who are at high risk for development of chronic Q fever include persons with preexisting valvular heart disease, vascular grafts, or arterial aneurysms.
- Infection during pregnancy and immunosuppression (e.g., from chemotherapy) are both conditions that have been linked to chronic Q fever development.
- Endocarditis and infections of aneurysms or vascular prostheses are the most common forms of chronic Q fever and generally are fatal if untreated.
- Chronic Q fever is rarely reported in children.
- In contrast with adults, osteomyelitis is one of the most common findings in children with pediatric chronic Q fever.

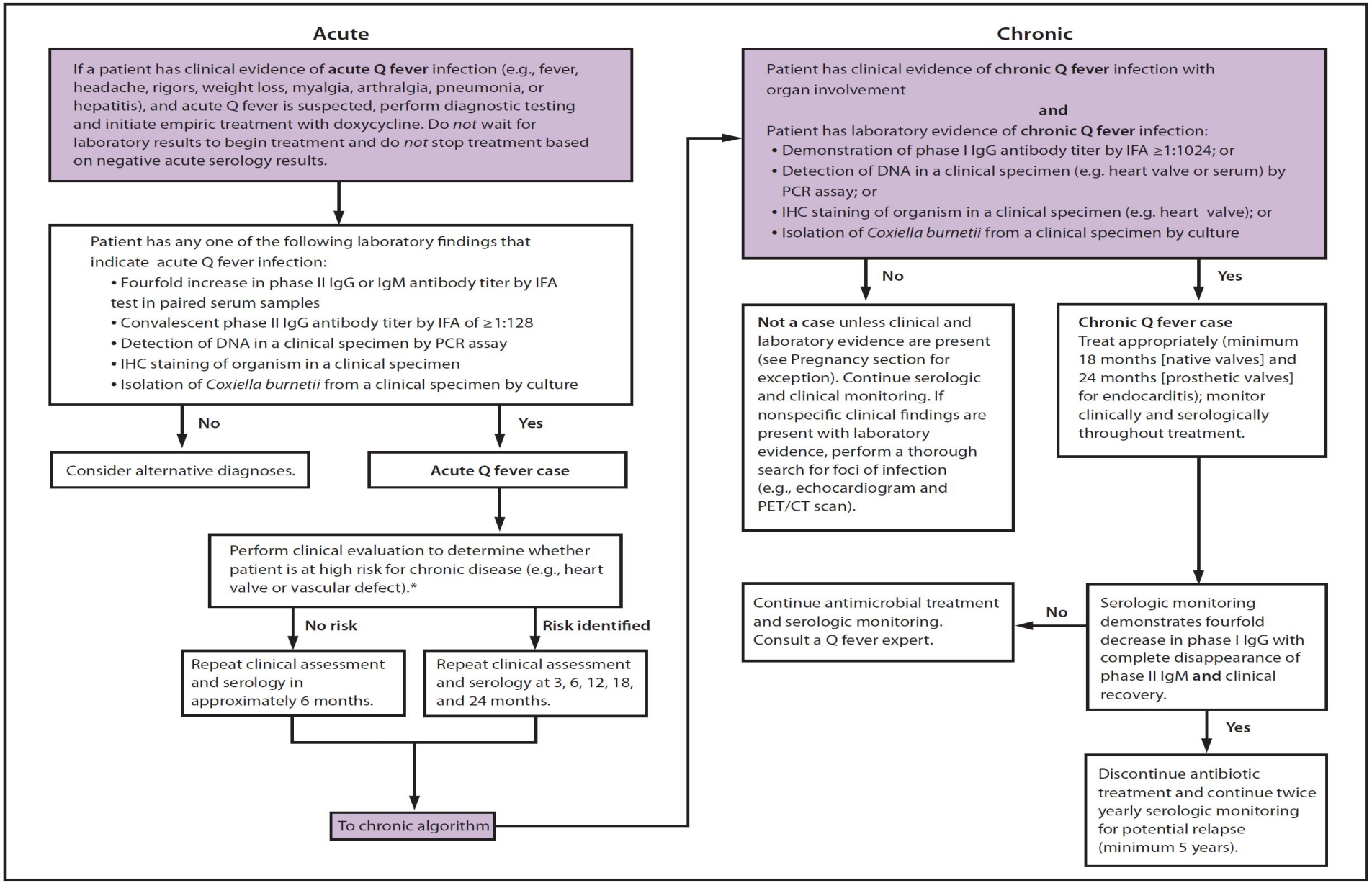
Q Fever Diagnostic Testing

TABLE 4. Types of Q fever diagnostic testing analyses, by phase of infection, type of sample, and interval since onset of symptoms

Phase of infection and type of sample	Interval since onset of symptoms	Type of analysis
Acute		
Whole blood	Until day 14 (and before antibiotic therapy)	PCR
Serum	Until day 21 for IFA	IFA for phase I and II IgG and IgM; PCR
	Until day 14 for PCR (and before antibiotic therapy)	
Convalescent		
Serum	3–6 weeks after acute sample	IFA for phase I and II IgG and IgM
Chronic		
Whole blood	>6 weeks after acute illness	PCR
Serum	>6 weeks after acute illness	IFA for phase I and II IgG and IgM; PCR
Heart valve and other tissues	6 weeks to years	PCR, culture, IHC

Abbreviations: IFA = immunofluorescent assay; IgG = immunoglobulin G; IgM = immunoglobulin M; IHC = immunohistochemistry; PCR = polymerase chain reaction.

FIGURE. Q fever management algorithm*



Abbreviations: CT = computed tomography; IFA = immunofluorescent assay; IgG = immunoglobulin G; IgM = immunoglobulin M; IHC = immunohistochemistry; PCR = polymerase chain reaction; PET = positron emission tomography.

* This algorithm is intended for use as a general guide and does not replace the physician's clinical judgment. It is intended to provide a management strategy for patients under the care of a physician and is not intended for those who might be tested for Q fever as part of an occupational monitoring program. Women infected during pregnancy should be treated and monitored as described in the text of the report.

TABLE 2. Recommended antibiotics and dosages* for treatment of acute and chronic Q fever

Indication	Adults	Children¶	Pregnant women
Acute Q fever†	Doxycycline§ 100 mg twice a day for 14 days	≥8 years: Doxycycline: 2.2 mg/kg per dose twice a day for 14 days (maximum 100 mg per dose) <8 years with high risk criteria**: Doxycycline: 2.2 mg/kg per dose twice a day for 14 days (maximum: 100 mg per dose) <8 years with mild or uncomplicated illness: Doxycycline 2.2 mg/kg per dose twice a day for 5 days (maximum 100 mg per dose). If patient remains febrile past 5 days of treatment: trimethoprim/sulfamethoxazole 4–20 mg/kg twice a day for 14 days (maximum: 800 mg per dose)	Trimethoprim/sulfamethoxazole: 160 mg/800 mg twice a day throughout pregnancy††
Chronic Q fever			
Endocarditis or vascular infection	Doxycycline§§ 100 mg twice a day and hydroxychloroquine¶¶ 200 mg three times a day ≥18 months	Recommend consultation***	Recommend consultation†††
Noncardiac organ disease§§§	Doxycycline 100 mg twice a day and hydroxychloroquine 200 mg three times a day	Recommend consultation***	Recommend consultation†††
Postpartum¶¶¶ with serologic profile for chronic Q fever	Doxycycline 100 mg twice a day and hydroxychloroquine 200 mg three times a day for 12 months	—	—
Post-Q fever fatigue syndrome****	No current recommendations	No current recommendations	No current recommendations

Q Fever in U.S. Military

Table. Postdeployment serum antibody titers to phase II antigen for Q fever in 8 US military personnel who served in Iraq, March 1–August 20, 2003*

Patient	IgG	IgM
1	1:1,024	Negative
2	1:128	Negative
3	>1:1,024	1:512
4	1:256	1:256
5	1:512	>1:1,024
6	1:512	1:512
7	1:64	1:64
8	>1:1,024	>1:1,024

*All predeployment titers were negative for immunoglobulin (Ig) G and IgM.

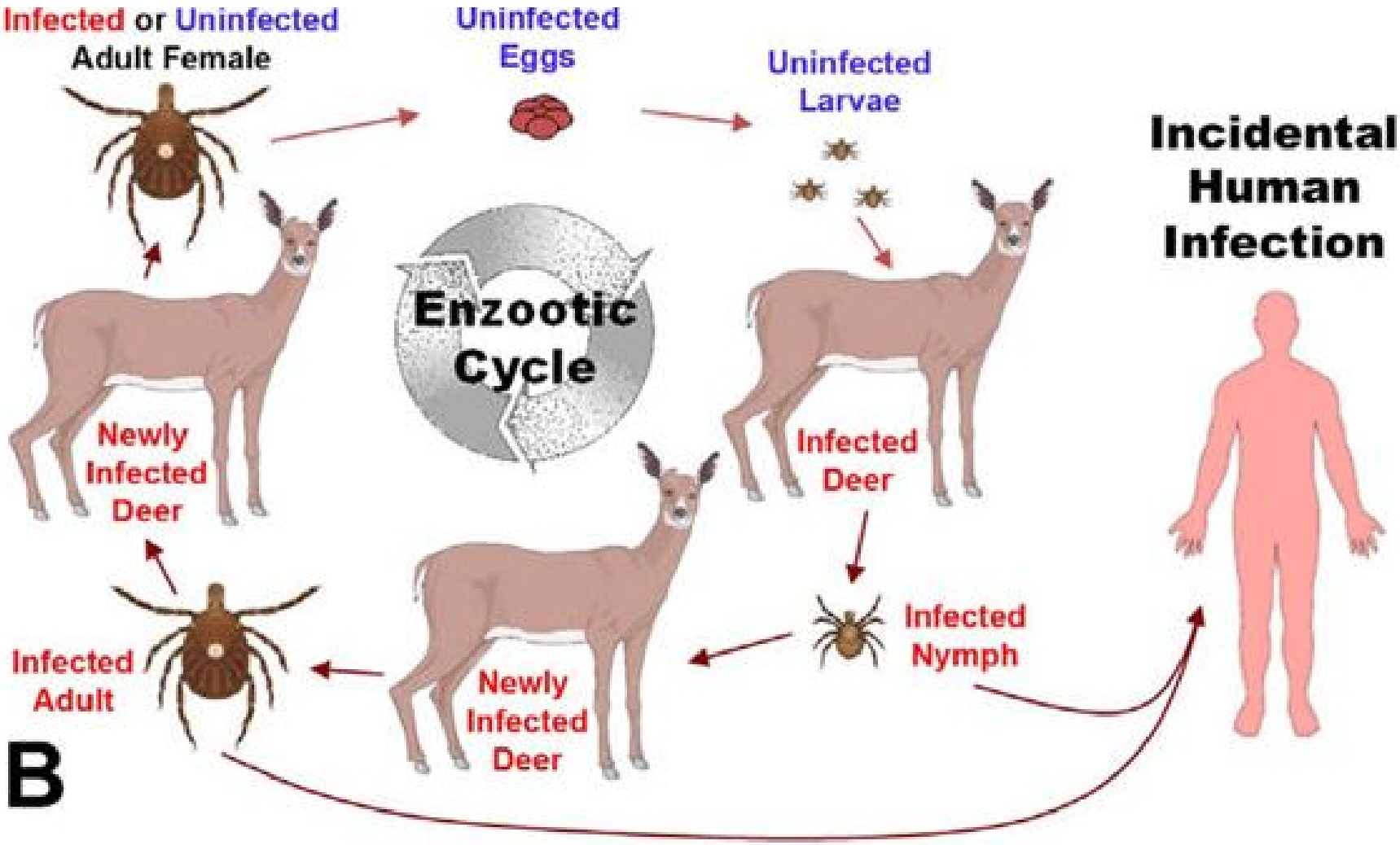
Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 11, No. 8, August 2005

Ehrlichiosis and anaplasmosis

Characteristic	HME	HGA	*E ewingii* ehrlichiosis
Year first reported	1987	1994	1999
Causative agent	*Ehrlichia chaffeensis*	*Anaplasma phagocytophilum*	*E ewingii*
Target leukocyte	Monocyte Macrophage	Granulocyte	Granulocyte
Reported cases	> 1603	> 2135	~20
Endemic range	South central Southeast Mid-Atlantic	Northeast Upper Midwest Pacific coast	South central
Tick vector	*Amblyomma americanum*	*Ixodes scapularis*, *Ixodes pacificus*	*A americanum*

HME, human monocytotropic ehrlichiosis; HGA, human granulocytotropic anaplasmosis.

HME rarely reported in Asia (Thailand); HGA in Western / Central Europe



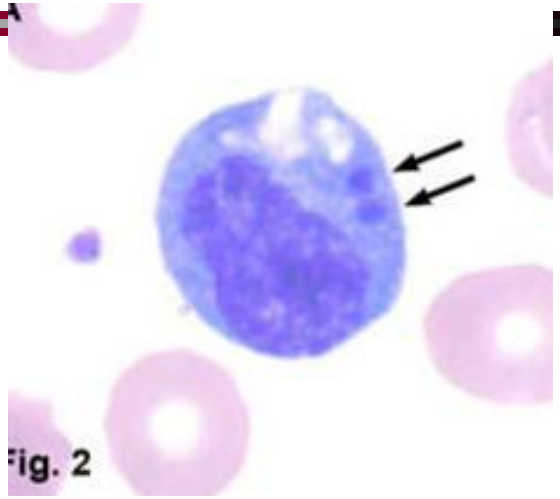
Clin Lab Med. 2010 March ; 30(1): 261–292. doi:10.1016/j.cll.2009.10.004.

Disease symptoms

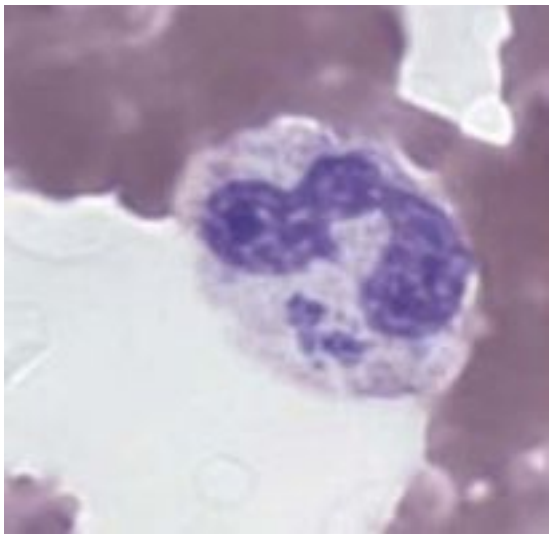
Symptom, sign, or finding	Patients, % (no. evaluated) HME	HGA
Symptom or sign		
Fever	97 (633)	93 (521)
Myalgia	57 (250)	77 (516)
Headache	80 (240)	76 (385)
Malaise	82 (234)	94 (288)
Nausea	64 (143)	38 (258)
Vomiting	33 (192)	26 (90)
Diarrhea	23 (197)	16 (95)
Cough	26 (155)	19 (260)
Arthralgias	41 (211)	46 (504)
Rash	31 (286)	6 (357)
Stiff neck	3 (240)	21 (24)
Confusion	19 (279)	17 (211)
Laboratory finding		
Leukopenia	62 (276)	49 (336)
Thrombocytopenia	71 (247)	71 (336)
Elevated serum AST or ALT level	83 (276)	71 (177)

CID, 2007

HME / HGA



- Incubation 5-14 days
- Rash rare; NO vasculitis
- Ecology of exposure:
  - HME: grassy areas, forest edge, un-mowed areas
  - Anaplasma: similar (May-Sept in USA)
- Diagnosis: paired serology
- Morulae = cytoplasmic inclusions
- Treatment:
  - doxycycline 100mg BID
  - 3d after afebrile (~5-7 days)
- Prevention: PPE



Ehrlichiosis

HME	HGA	*E. ewingii*
1987	1994	1999
E. chaffeensis	*A. Phagocytophilum*	*E. ewingii*
Monocyte macrophage	Granulocyte	Granulocyte
>1600	>2100	~20
SC, SE, mid-Atl	NE, MW, Pac coast	SC (S. central)

Military importance (Ehrlichiosis)

Group, disease	Causative agent	Mode	Geographic
Canine	*E. canis*	Tick bite	SE Asia, SW US, Venezuela
HME	*E. chaffeensis*	Tick bite	Americas, Europe, Thailand
HGA	*A. phagocytophilum*	Tick bite	USA, Europe, Asia
Sennetsu fever	*Neorickettsia sennetsu*	unknown	Japan, Malaysia

CID, 2002

Ehrlichia – disease symptoms

Symptom, sign, or finding	Patients, % (no. evaluated) HME	HGA
Symptom or sign		
Fever	97 (633)	93 (521)
Myalgia	57 (250)	77 (516)
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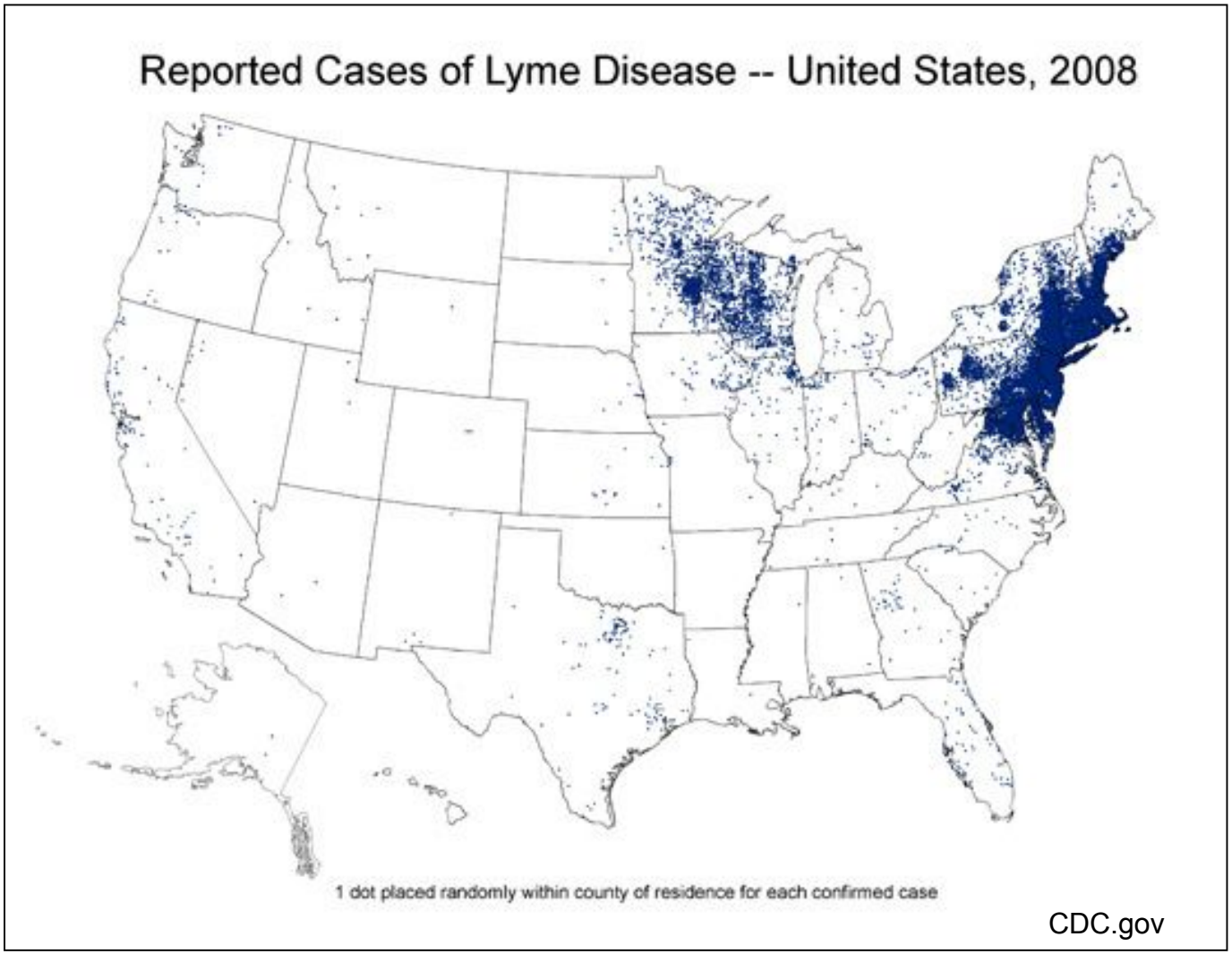
CID, 2007

Ehrlichiosis

- Incubation 5-14 days
- Rash rare; NO vasculitis
- Ecology of exposure:
  - HME: grassy areas, forest edge, un-mowed areas
  - Anaplasma: similar (May-Sept in USA)
- Diagnosis: paired serology; morulae=cytoplasmic inclusions
- Treatment: doxycycline 100mg BID ~ 3d after afebrile (~5-7 days)
- Prevention: PPE

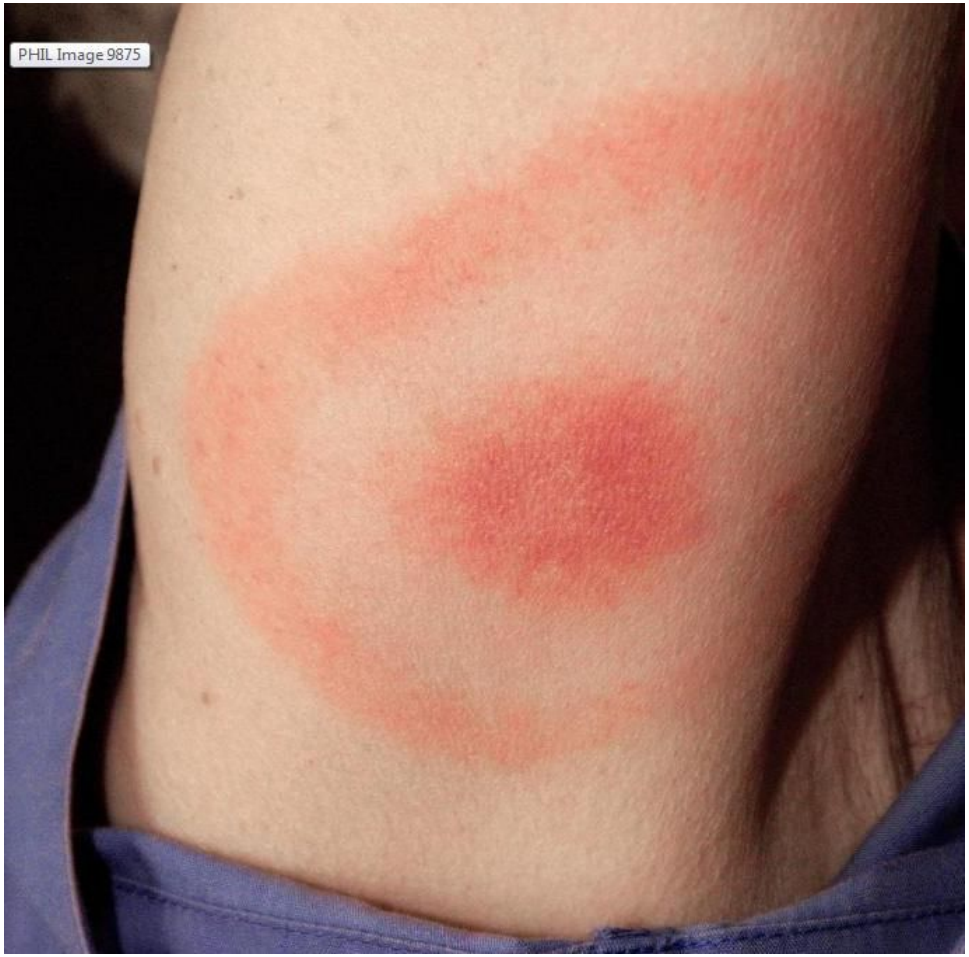
Lyme disease (*B. borgdorferi*)



Common presenting symptoms

- Rash ~ 70-80% of infected persons
  - Begins at the site of a tick bite after a delay of 3-30 days
  - Gradually expands over a period of several days, reaching up to 12 inches (30 cm) across
  - Center of the rash may clear as it enlarges (Bull's-eye). It may be warm but not usually painful. Some patients develop additional EM lesions in other areas of the body after several days.
- +/- fatigue, chills, fever, headache, and muscle and joint aches, and swollen lymph nodes
- In context of outdoor exposure

Lyme disease (*B. borgdorferi*)



CDC.gov

Lyme disease (*B. borgdorferi*)

Treatment:

- Erythema migrans: doxycycline 100mg PO BID (10-14 days)
- Meningitis or radiculopathy: ceftriaxone x 14 days (range 10-28 days)
- Cranial nerve palsy: doxy x 14 days (range 14-21 days), some use parenteral regimen especially if abnl CSF seen
- Cardiac disease: oral or parenteral regimen 14 days (range 14-21 days)
- Arthritis (late lyme disease):oral regimen 28 days
- Recurrent arthritis after oral regimen: repeat oral 28 days course or parenteral regimen 14-28 days
- CNS or peripheral nervous system disease: parenteral regimen 14 days (range 14-28 days)
- Acrodermatitis chronica atrophicans(seen mostly in Europe): oral regimen 21 days (14-28 days)

Prevention:

PPE (tick checks, permethrin, DEET, doxy 200mg x1 within 72hrs)